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By Gordon B. Parker, Elaine A. Barrett, and Ian B. Hickie

Official Journal of the American Psychiatric Association

1. Based on independent market research data, December 1988-April 1992.

Prozac®

fluoxetine hydrochloride

Brief Summary. Consult the package insert for complete prescribing information.

Indication: For the treatment of depression.

Contraindications: Known hypersensitivity to Prozac.

Monamine Oxidase Inhibitors — There have been reports of serious, sometimes fatal, reactions in patients receiving fluoxetine in combination with an MAOI and in patients who have recently discontinued fluoxetine and are then started on an MAOI. Some cases presented with features resembling neuroleptic malignant syndrome.

Wait at least 14 days between discontinuing an MAOI and starting therapy with Prozac. Because of the long half-lives of fluoxetine and its active metabolite, wait at least 5 weeks between discontinuing Prozac and starting therapy with an MAOI. Prozac should not be used concomitantly with MAOIs.

Warnings: Rash and Possibly Allergic Events — Approximately 4% of 5,600 fluoxetine patients developed a rash and/or urticaria in premarketing testing. Almost a third of these discontinued therapy because of rash and/or associated systemic signs or symptoms. Reported in association with rash were fever, leukocytosis, arthralgias, edema, carpal tunnel syndrome, respiratory distress, lymphadenopathy, proteinuria, and mild transaminase elevation. Most patients improved promptly upon discontinuation of fluoxetine and/or adjunctive treatment with antihistamines or steroids, and all were reported to recover completely.

Of 2 patients who developed a serious cutaneous systemic illness during premarketing clinical trials, 1 was considered to have a leukocytoclastic vasculitis, and the other, a severe desquamating syndrome considered variously to be a vasculitis or erythema multiforme. Other patients have had systemic syndromes suggestive of serum sickness.

Since the introduction of Prozac, systemic events possibly related to vasculitis have developed in patients with rash. Although these events are rare, they may be serious, involving the lung, kidney, or liver. Death has been reported to occur in association with these systemic events.

Anaphylactoid events, including bronchospasm, angioedema, and urticaria alone and in combination, have been reported.

Pulmonary events, including inflammatory processes of varying histopathology and/or fibrosis, have been reported rarely. These events have occurred with dyspnea as the only preceding symptom.

Whether these systemic events and rash have a common underlying cause or represent immunologic responses is not known. Upon the appearance of rash or of other possibly allergic phenomena for which an alternative etiology cannot be identified, Prozac should be discontinued.

Precautions: General — **Anxiety, Nervousness, and Insomnia** — Reported by 10% to 15% of patients, 5% of whom discontinued fluoxetine.

Altered Appetite and Weight — Significant weight loss, especially in underweight patients, may be an undesirable result of treatment.

Approximately 9% of fluoxetine patients experienced anorexia in controlled clinical trials, an incidence approximately sixfold that seen with placebo. A weight loss >5% of body weight occurred in 13% of fluoxetine patients compared with 4% in those on placebo and 3% in those on tricyclics. However, only rarely did fluoxetine patients discontinue treatment because of weight loss.

Activation of Mania/Hypomania — Hypomania or mania occurred in approximately 1% of fluoxetine patients in premarketing testing.

Seizures — Twelve of 6,000 patients (0.2%) experienced convulsions (or, possibly, seizures). Prozac should be introduced with care in patients with a history of seizures.

Suicide — Close supervision of high-risk patients should accompany initial therapy. Prescriptions of Prozac should be written for the smallest quantity of capsules consistent with good patient management to reduce the risk of overdose.

The Long Elimination Half-Lives of Fluoxetine and Its Metabolites — Because of the long elimination half-lives of the parent drug (2 to 3 days) and its major active metabolite (7 to 9 days), changes in dose will not be fully reflected in plasma for several weeks, affecting both strategies for titration to final dose and withdrawal from treatment.

Use in Patients with Concomitant Illness — Caution is advisable in patients with diseases or conditions that could affect metabolism or hemodynamic responses.

Fluoxetine has not been evaluated or used to any appreciable extent in patients with a recent history of myocardial infarction or unstable heart disease. ECGs of 312 patients who received Prozac in double-blind trials were retrospectively evaluated; no conduction abnormalities that resulted in heart block were observed. The mean heart rate was reduced by approximately 3 beats/min.

In subjects with cirrhosis, the clearances of fluoxetine and its active metabolite were decreased. A lower or less frequent dose should be used in patients with cirrhosis.

Fluoxetine should be used with caution in patients with severe renal impairment.

In patients with diabetes, Prozac may alter glycemic control. Hypoglycemia has occurred during therapy with Prozac, and hyperglycemia has developed following discontinuation. Insulin and/or oral hypoglycemic dosage may need to be adjusted when fluoxetine therapy is instituted or discontinued.

Interference with Cognitive and Motor Performance — Any psychoactive drug may impair judgment, thinking, or motor skills, and patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that the drug does not affect them adversely.

Information for Patients — Physicians should advise their patients to notify them if they:

- are taking or plan to take any prescription or over-the-counter drugs or alcohol
- become pregnant or intend to become pregnant during therapy
- are breast feeding an infant
- develop a rash or hives

Drug Interactions — **Tryptophan** — Five patients receiving tryptophan experienced adverse reactions, including agitation, restlessness, and gastrointestinal distress.

Monamine Oxidase Inhibitors — See Contraindications.

Other Antidepressants — There have been greater than 2-fold increases of previously stable plasma levels of other antidepressants when Prozac has been administered in combination with these agents.

Lithium — There have been reports of both increased and decreased lithium levels and lithium toxicity. Lithium levels should be monitored.

Diazepam Clearance — The half-life of diazepam may be prolonged in some patients.

Drugs Tightly Bound to Plasma Proteins — Because fluoxetine is tightly bound to plasma protein, the concurrent administration of fluoxetine and another tightly bound drug may cause a shift in plasma concentrations potentially resulting in an adverse effect. Adverse effects may also result from displacement of protein-bound fluoxetine by other tightly bound drugs.

CNS-Active Drugs — Caution is advised if the concomitant administration of Prozac and such drugs is required.

Electroconvulsive Therapy — There have been rare reports of prolonged seizures in patients on fluoxetine receiving ECT treatment.

Carcinogenesis, Mutagenesis, Impairment of Fertility — There is no evidence of carcinogenicity, mutagenicity, or impairment of fertility with Prozac.

The dietary administration of fluoxetine to rats and mice for 2 years at doses approximately 7.5 and 9.0 times the maximum human dose (80 mg) respectively revealed no evidence of carcinogenicity.

Fluoxetine and norfluoxetine have been shown to have no genotoxic effects based on the following assays: bacterial mutation assay, DNA repair assay in cultured rat hepatocytes, mouse lymphoma assay, and in vivo sister chromatid exchange assay in Chinese hamster bone marrow cells.

Two fertility studies in rats at doses approximately 5 and 9 times the maximum human dose (80 mg) respectively revealed no adverse effects on fertility. A slight decrease in neonatal survival was noted, probably associated with depressed maternal food consumption and suppressed weight gain.

Pregnancy — **Teratogenic Effects** — **Pregnancy Category B** — Reproduction studies in rats and rabbits at doses 9 and 11 times the maximum human dose (80 mg) respectively revealed no evidence of harm to the fetus. Although there have been no adequate and well-controlled studies in pregnant women, this drug should be used during pregnancy only if clearly needed.

Labor and Delivery — The effect of Prozac on labor and delivery in humans is unknown.

Nursing Mothers — Because Prozac is known to be excreted in human milk, caution should be exercised when Prozac is administered to a nursing woman.

Use in Children — Safety and effectiveness in children have not been established.

Use in the Elderly — In clinical studies of several hundred elderly patients, no unusual adverse age-related phenomena were identified. However, these data are insufficient to rule out possible age-related differences during chronic use, particularly in elderly patients with concomitant systemic illnesses or those receiving concomitant drugs.

Hypotension — Hypotension (some cases with serum Na <110 mmol/L) has been reported, which appeared to be reversible on drug discontinuation. Some cases were possibly due to SIAHD, and the majority have been in older patients and those taking diuretics or otherwise volume depleted.

Platelet Function — There have been rare reports of altered platelet function and/or abnormal results from laboratory studies in patients taking fluoxetine. While there have been reports of abnormal bleeding in several patients taking fluoxetine, it is unclear whether fluoxetine had a causative role.

Adverse Reactions: Commonly Observed — Nervous system complaints, including anxiety, nervousness, and insomnia; drowsiness and fatigue or asthenia; tremor; sweating; gastrointestinal complaints, including anorexia, nausea, and diarrhea; and dizziness or lightheadedness.

Associated With Discontinuation of Treatment — Fifteen percent of 4,000 clinical trial patients discontinued fluoxetine due to an adverse event. The more common events included: psychiatric (5.3%), primarily nervousness, anxiety, and insomnia; digestive (3.0%), primarily nausea; nervous system (1.6%), primarily dizziness; body as a whole (1.5%), primarily asthenia and headache; and skin (1.4%), primarily rash and pruritus.

Incidence in Controlled Clinical Trials — The accompanying table enumerates adverse events that occurred at a frequency of $\geq 1\%$ in controlled trials.

Other Events Observed During Premarketing Evaluation in 5,600 Fluoxetine Patients — Frequent adverse events are defined as those occurring on 1 or more occasions in at least 1/100 patients; infrequent adverse events are those occurring in 1/100 to 1/1,000 patients; rare events are those occurring in less than 1/1,000 patients.

Body as a Whole — **Frequent:** chills; **Infrequent:** chills and fever, cyst, face edema, hangover effect, jaw pain, malaise, neck pain, neck rigidity, and pelvic pain; **Rare:** abdomen enlarged, callusitis, hydrocephalus, hypothermia, LE syndrome, moniliasis, and serum sickness.

Cardiovascular System — **Infrequent:** angina pectoris, arrhythmia, hemorrhage, hypertension, hypotension, migraine, postural hypotension, syncope, and tachycardia; **Rare:** AV block first-degree, bradycardia, bundle branch block, cerebral ischemia, myocardial infarct, thrombophlebitis, vascular headache, and ventricular arrhythmia.

Digestive System — **Frequent:** increased appetite; **Infrequent:** aphthous stomatitis, dysphagia, eructation, esophagitis, gastritis, gingivitis, glossitis, liver function tests abnormal, melena, stomatitis, thirst; **Rare:** bloody diarrhea, cholecystitis, cholelithiasis, colitis, duodenal ulcer, enteritis, fecal incontinence, hematemesis, hepatitis, hepatomegaly, hyperchlorhydria, increased salivation, jaundice, liver tenderness, mouth ulceration, salivary gland enlargement, stomach ulcer, tongue discoloration, and tongue edema.

Endocrine System — **Infrequent:** hypothyroidism; **Rare:** goiter and hyperthyroidism.

Hemic and Lymphatic System — **Infrequent:** anemia and lymphadenopathy; **Rare:** bleeding time increased, blood dyscrasia, leukopenia, lymphocytosis, petechia, purpura, sedimentation rate increased, and thrombocytopenia.

Metabolic and Nutritional — **Frequent:** weight loss; **Infrequent:** generalized edema, hypoglycemia, peripheral edema, and weight gain; **Rare:** dehydration, gout, hypercholesterolemia, hyperglycemia, hyperlipemia, hypoglycemic reaction, hypokalemia, hyponatremia, and iron deficiency anemia.

Musculoskeletal System — **Infrequent:** arthritis, bone pain, bursitis, tenosynovitis, and twitching; **Rare:** bone necrosis, chondrodysplasia, muscle hemorrhage, myositis, osteoporosis, pathological fracture, and rheumatoid arthritis.

Nervous System — **Frequent:** abnormal dreams and agitation; **Infrequent:** abnormal gait, acute brain syndrome, akathisia, amnesia, apathy, ataxia, buccoglossal syndrome, CNS stimulation, convulsion,

TREATMENT-EMERGENT ADVERSE EXPERIENCE INCIDENCE IN PLACEBO-CONTROLLED CLINICAL TRIALS

Body System/ Adverse Event*	Percentage of Patients Reporting Event		Percentage of Patients Reporting Event	
	Prozac (N = 1,730)	Placebo (N = 799)	Prozac (N = 1,730)	Placebo (N = 799)
Nervous	20.3	15.5	Body as a Whole	
Headache	14.9	8.5	Althia	4.4
Nervousness	13.8	7.1	Infection, viral	3.4
Insomnia	11.6	6.3	Pain, limb	1.6
Drowsiness	9.4	5.5	Fever	1.4
Anxiety	7.9	2.4	Pain, chest	1.3
Tremor	5.7	3.3	Allergy	1.2
Dizziness	4.2	1.1	Influenza	1.2
Fatigue	1.9	1.3	Respiratory	
Sensation	1.7	2.0	Respiratory	
disturbance	1.6	—	Infection	7.6
Lbido,	1.6	—	Flu-like	6.0
decreased	1.6	—	Syndrome	2.8
Light-	1.6	—	Pharyngitis	1.9
headedness	1.5	—	Nasal	2.7
Concentration,	1.5	—	congestion	2.6
decreased	21.1	10.1	Headache,	2.3
Digestive	12.3	7.0	sinus	2.6
Nausea	9.5	6.0	Sinusitis	2.1
Diarrhea	8.7	1.5	Cough	2.0
Mouth	6.4	4.3	Dyspepsia	1.6
dryness	4.5	3.3	Odynia	1.4
Anorexia	3.7	1.5	Cardiovascular	
Dyspepsia	4.4	4.3	Hot flashes	1.8
Constipation	1.6	1.1	Palpitations	1.3
Pain,	3.4	2.9	Musculoskeletal	
abdominal	2.4	1.3	Pain, back	2.0
Vomiting	1.5	—	Pain, joint	1.2
Taste change	1.6	1.1	Pain, muscle	1.2
Flatulence	1.0	1.4	Urinary	
Gastroenteritis	8.4	3.8	Infection	1.9
Skin and	2.7	1.8	Menstruation,	1.4
Appendages	2.4	1.4	painful	
Sweating,	—	—	Sexual	
excessive	—	—	dysfunction	1.9
Rash	—	—	Frequent	
Pruritus	—	—	itching	1.6
			Urinary tract	—
			Infection	1.2
			Special Senses	
			Vision	
			disturbance	2.8
				1.8

*Events reported by $\geq 1\%$ of fluoxetine patients are included.
— Incidence <1%.

delusions, depersonalization, emotional lability, euphoria, hallucinations, hostility, hyperkinesia, hyposthesia, incoordination, libido increased, manic reaction, neuralgia, neuropathia, paranoid reaction, psychosis, and vertigo; **Rare:** abnormal electroencephalogram, anti-social reaction, chronic brain syndrome, circumoral paresthesia, CNS depression, coma, dysarthria, dystonia, extrapyramidal syndrome, hypertonia, hysteria, myoclonus, nystagmus, paralysis, reflexes decreased, stupor, and torticollis.

Respiratory System — **Frequent:** bronchitis, rhinitis, and yawn; **Infrequent:** asthma, epistaxis, hiccup, hyperventilation, and pneumonia; **Rare:** apnea, hemoptysis, hypoxia, larynx edema, lung edema, lung fibrosis/atelectasis, and pleural effusion.

Skin and Appendages — **Infrequent:** acne, alopecia, contact dermatitis, dry skin, herpes simplex, maculopapular rash, and urticaria; **Rare:** eczema, erythema multiforme, fungal dermatitis, herpes zoster, hirsutism, psoriasis, purpuric rash, pustular rash, seborrhea, skin discoloration, skin hypertrophy, subcutaneous nodule, and vesiculobullous rash.

Special Senses — **Infrequent:** amblyopia, conjunctivitis, ear pain, eye pain, mydriasis, photophobia, and tinnitus; **Rare:** blepharitis, cataract, corneal lesion, deafness, diplopia, eye hemorrhage, glaucoma, iritis, ptosis, strabismus, and taste loss.

Urogenital System — **Infrequent:** abnormal ejaculation, amenorrhea, breast pain, cystitis, dysuria, fibrocystic breast, impotence, leukorrhea, menopause, menorrhagia, ovarian disorder, urinary incontinence, urinary retention, urinary urgency, urination impaired, and vaginitis; **Rare:** abortion, albuminuria, breast enlargement, dyspareunia, epididymitis, female lactation, hematuria, hypomenorrhea, kidney calculus, metrorrhagia, orchitis, polyuria, pyelonephritis, pyuria, salpingitis, urethral pain, urethritis, urinary tract disorder, urolithiasis, uterine hemorrhage, uterine spasm, and vaginal hemorrhage.

Postintroduction Reports — Voluntary reports of adverse events temporally associated with Prozac that have been received since market introduction and which may have no causal relationship with the drug include the following: aplastic anemia, cerebral vascular accident, confusion, dyskinesia (including, for example, a case of buccal-lingual-masticatory syndrome with involuntary tongue protrusion reported to develop in a 77-year old female after 5 weeks of fluoxetine therapy and which completely resolved over the next few months following drug discontinuation), ecchymoses, eosinophilic pneumonia, gastrointestinal hemorrhage, hyperprolactinemia, immune-related hemolytic anemia, movement disorders developing in patients with risk factors including drugs associated with such events and worsening of preexisting movement disorders, neuroleptic malignant syndrome-like events, pancreatitis, pancytopenia, suicidal ideation, thrombocytopenia, thrombotic purpura, vaginal bleeding after drug withdrawal, and violent behaviors.

Overdose: Human Experience — As of December 1987, there were 2 deaths among approximately 38 reports of acute overdose with fluoxetine, either alone or in combination with other drugs and/or alcohol. One death involved a combined overdose with approximately 1,800 mg of fluoxetine and an undetermined amount of meprobamate. A second death involved fluoxetine, codeine, and temazepam.

One other patient who reportedly took 3,000 mg of fluoxetine experienced 2 grand mal seizures that remitted spontaneously without specific anticonvulsant treatment. The actual amount of drug absorbed may have been less due to vomiting.

Nausea and vomiting were prominent in overdoses involving high fluoxetine doses. Other prominent symptoms of overdose included agitation, restlessness, hypomania, and other signs of CNS excitation. Except for the 2 deaths noted above, all other overdose cases recovered without residua.

Since introduction, reports of death attributed to overdose of fluoxetine alone have been extremely rare.

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Additional information available to the profession upon request.



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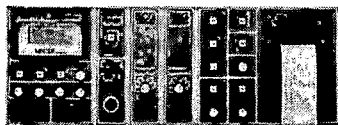
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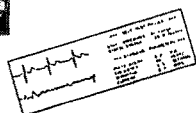
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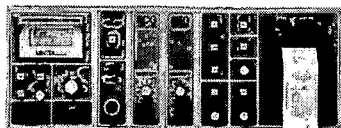
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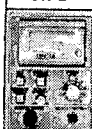
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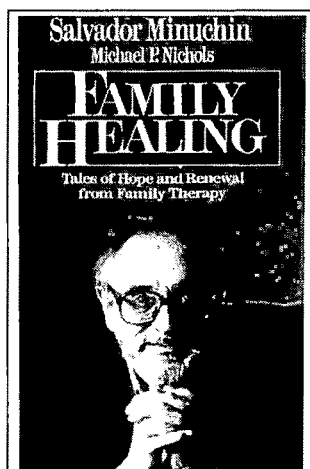
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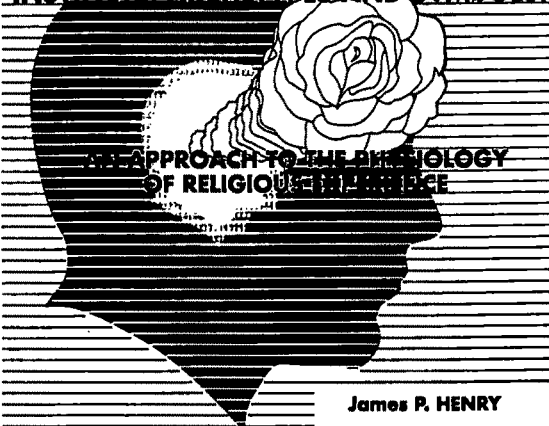
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WARNING

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INDICATIONS

Treatment of manic episodes of manic-depressive illness. Maintenance therapy prevents or diminishes the intensity of subsequent episodes in those manic-depressive patients with a history of mania.

WARNINGS

Lithium should generally not be given to patients with significant renal or cardiovascular disease, severe debilitation or dehydration, or sodium depletion.

Chronic lithium therapy may be associated with diminution of renal concentrating ability. Such patients should be carefully managed to avoid dehydration with resulting lithium retention and toxicity. Morphologic changes with glomerular and interstitial fibrosis and nephron atrophy have been reported. Morphologic changes have also been seen in manic-depressive patients never exposed to lithium. During lithium therapy, progressive or sudden changes in renal function, even within the normal range, indicate the need for reevaluation of treatment.

An encephalopathic syndrome [characterized by weakness, lethargy, fever, tremulousness and confusion, extrapyramidal symptoms, leukocytosis, elevated serum enzymes, BUN and FBG] has occurred in a few patients treated with lithium plus a neuroleptic. In some instances, the syndrome was followed by irreversible brain damage. Patients receiving such combined therapy should be monitored closely for early evidence of neurologic toxicity and treatment discontinued promptly if such signs appear. Caution patients about activities requiring alertness.

Lithium may prolong the effects of neuromuscular blocking agents. Such agents should be given with caution to patients receiving lithium.

Lithium carbonate may cause fetal harm when administered to a pregnant woman. If a patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

Nursing should not be undertaken during lithium therapy except in rare and unusual circumstances.

Not recommended in children under 12.

Elderly patients often require lower lithium dosages to achieve therapeutic serum levels. They may also exhibit adverse reactions at serum levels ordinarily tolerated by younger patients.

PRECAUTIONS

Caution should be used when lithium and diuretics are used concomitantly. Patients receiving such combined therapy should have serum lithium levels monitored closely and the lithium dosage adjusted if necessary.

Sweating, diarrhea and concomitant infection with elevated temperatures may also necessitate a temporary reduction or cessation of medication.

Indomethacin and piroxicam have been reported to increase significantly, steady state plasma lithium levels. There is also some evidence that other nonsteroidal anti-inflammatory agents may have a similar effect. When such combinations are used, increased plasma lithium level monitoring is recommended. Concurrent use of metronidazole with lithium may provoke lithium toxicity due to reduced renal clearance. Monitor patients receiving such combined therapy closely.

When used with angiotensin-converting enzyme inhibitors, such as enalapril and captopril, lithium dosage may need to be decreased; measure plasma lithium levels more often.

Concurrent use of calcium channel blocking agents with lithium may increase the risk of neurotoxicity in the form of ataxia, tremors, nausea, vomiting, diarrhea and/or tinnitus. Caution is recommended.

ADVERSE REACTIONS

Adverse reactions may be encountered at serum lithium levels below 1.5 mEq/L. Mild to moderate adverse reactions may occur at levels from 1.5 to 2.5 mEq/L, and moderate to severe reactions may be seen at levels of 2.0 mEq/L and above. Fine hand tremor, polyuria and mild thirst may occur during initial therapy and may persist throughout treatment. Transient and mild nausea and general discomfort may also appear during initial therapy. These side effects usually subside with continued treatment or a temporary reduction or cessation of dosage. Diarrhea, vomiting, drowsiness, muscular weakness and lack of coordination may be early signs of lithium intoxication, and can occur at lithium levels below 2.0 mEq/L. At higher levels, ataxia, giddiness, tinnitus, blurred vision and a large output of dilute urine may be seen. Serum lithium levels above 3.0 mEq/L may produce a complex clinical picture, involving multiple organs and organ systems. Serum lithium levels should not be permitted to exceed 2.0 mEq/L during the acute treatment phase.

The following reactions appear to be related to serum lithium levels, including levels within the therapeutic range. **Neuromuscular/Central Nervous System**—tremor, muscle hyperirritability (fasciculations, twitching, clonic movements of whole limbs), hyperreflexia, ataxia, choreo-athetoid movements, hyperactive deep tendon reflex, extrapyramidal symptoms including acute dystonia, cogwheel rigidity, blackout spells, epileptiform seizures, slurred speech, dizziness, vertigo, downbeat nystagmus, incontinence of urine or feces, somnolence, psychomotor retardation, restlessness, confusion, stupor, coma, tongue movements, tics, tinnitus, hallucinations, poor memory, slowed intellectual functioning, started response, worsening of organic brain syndromes. **Cardiovascular**—cardiac arrhythmia, hypotension, peripheral circulatory collapse, bradycardia, sinus node dysfunction with severe bradycardia [which may result in syncope]; **Gastrointestinal**—anorexia, nausea, vomiting, diarrhea, gastritis, salivary gland swelling, abdominal pain, excessive salivation, flatulence, indigestion; **Genitourinary**—glycosuria, decreased creatinine clearance, albuminuria, oliguria and symptoms of nephrogenic diabetes insipidus including polyuria, thirst and polydipsia; **Dermatologic**—drying and thinning of hair, alopecia, anesthesia of skin, acne, chronic folliculitis, xerosis cutis, psoriasis or its exacerbation, generalized pruritus with or without rash, cutaneous ulcers, angioedema; **Autonomic**—blurred vision, dry mouth, impotence/sexual dysfunction; **Thyroid Abnormalities**—euthyroid goiter and/or hypothyroidism [including myxedema] accompanied by lower T_3 and T_4 uptake may be elevated. [See PRECAUTIONS.] Paradoxically, rare cases of hyperthyroidism have been reported; **EKG Changes**—diffuse slowing, widening of the frequency spectrum, potentiation and disorganization of background rhythm; **EKG Changes**—reversible flattening, isoelectricity or inversion of T-waves; **Miscellaneous**—fatigue, lethargy, transient scotomata, exophthalmos, dehydration, weight loss, leukocytosis, headache, transient hyperglycemia, hypercalcemia, hyperparathyroidism, excessive weight gain, edematous swelling of ankles or wrists, metallic taste, dysgeusia/taste distortion, salty taste, thirst, swollen lips, tightness in chest, swollen and/or painful joints, fever, polyarthralgia, dental caries. Some reports of nephrogenic diabetes insipidus, hyperparathyroidism and hypothyroidism which persist after lithium discontinuation have been received.

A few reports have been received of the development of painful discoloration of fingers and toes and coldness of the extremities within one day of the starting of treatment with lithium. The mechanism through which these symptoms [resembling Raynaud's syndrome] developed is not known. Recovery followed discontinuance.

Cases of pseudotumor cerebri [increased intracranial pressure and papilledema] have been reported with lithium use. Lithium should be discontinued, if clinically possible, if this syndrome occurs.

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September 3-5, annual meeting, International Federation of Psychoanalytic Societies, Munich. Contact: Marja Lindqvist, F.M. Secretary-General, Lansitie 9, 02160 Espoo, Finland; 358-0-426425.

September 8-13, annual meeting, National Alliance for the Mentally Ill, Washington, D.C. Contact: Laurie M. Flynn, Executive Director, 2101 Wilson Blvd., Suite 302, Arlington, VA 22201; 703-524-7600.

September 11-12, national conference, "Psychosocial Oncology: Enhancing Patient and Family Care" (14 hours of CME category 1 credit), Beverly Hills, Calif. Contact: Deane L. Wolcott, M.D., the Cedars-Sinai Comprehensive Cancer Center, 8700 Beverly Blvd., Los Angeles, CA 90048; 310-855-5486.

September 11-14, annual meeting, Royal College of Physicians and Surgeons of Canada, Ottawa. Contact: Dr. G.D. Hurteau, Executive Director, 74 Stanley Avenue, Ottawa, Ont. K1M 1P4, Canada; 613-746-8177.

September 14-17, annual meeting, American College of Emergency Physicians, Seattle. Contact: Colin C. Rorrie, Jr., Ph.D., Executive Director, P.O. Box 619911, Dallas, TX 75261-9911; 214-550-0911.

September 15-18, 2nd International Symposium, "Serotonin: From Cell Biology to Pharmacology and Therapeutics," Baylor College of Medicine, Giovanni Lorenzini Medical Foundation, and the Serotonin Club, Houston. Contact: Giovanni Lorenzini Medical Foundation, Baylor College of Medicine, Room 826E, One Baylor Plaza, Houston, TX 77030; 713-797-0401 (tel), 713-796-8853 (fax).

September 16-18, annual meeting, Canadian Psychiatric Association, Montreal. Contact: Canadian Psychiatric Association, 294 Albert Street, Suite 204, Ottawa, Ont. K1P 6E6, Canada; 613-234-2815.

September 18-20, annual meeting, Epilepsy Foundation of America, Alexandria, Va. Contact: William M. McLin, Ex-

ecutive Vice-President, 4351 Garden City Drive, Landover, MD 20785; 301-459-3700.

September 23, annual meeting, American Board of Medical Specialties, Chicago. Contact: Donald G. Langsley, M.D., Executive Vice-President, One Rotary Center, Suite 805, Evanston, IL 60201; 708-491-9091.

September 24-25, annual meeting, American Academy of Medical Administrators, New Orleans. Contact: Thomas H. O'Donovan, Ph.D., President, 30555 Southfield Road, Suite 150, Southfield, MI 48076; 313-540-4310.

September 26-30, biennial international congress, "150 Years of Psychiatry," German Society for Psychiatry and Neurology, University of Cologne. Contact: Dr. Andreas Krah, Oberarzt der Klinik und Poliklinik für Neurologie und Psychiatrie der Universität zu Köln, Joseph Stelzmann Str. 9, 5000 Cologne 41, Germany; (country code) 221-4786357 (tel), (country code) 221-4786398 (fax).

September 27-30, annual meeting, Association of Mental Health Administrators, Cincinnati. Contact: Barbara A. Scott, Executive Director, 60 Revere Drive, Suite 500, Northbrook, IL 60062; 708-480-9626.

September 27-October 1, annual meeting, Royal Australian and New Zealand College of Psychiatrists, Canberra Australian Capital Territory. Contact: Margaret Ettridge, Assistant Registrar, P.O. Box 418, South Carlton, Victoria 3053, Australia; 03-6635466.

September 27-October 1, annual meeting, World Medical Association, Marbella, Spain. Contact: Angel Orozco, Executive Director, 28, Avenue des Alpes, 01210 Ferbet-Voltaire, France; 50-40-75-75.

September 30-October 4, annual meeting, Southern Psychiatric Association, Hot Springs, Va. Contact: Jeanette Stone, Manager of Affiliated Societies, 35 Lakeshore Dr., Birmingham, AL 35219; 205-945-8903.

OCTOBER

October 1-2, 3rd Annual Cultural Impact Conference, "Effective Interventions With Children, Adolescents, and Young Adults in the Context of Ethnocultural Diversity," Chicago School of Professional Psychology, Chicago. Contact: Sue Kulasingham, 312-786-9443.

(Continued on page A31)

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Sex With Former Patients Almost Always Unethical

While sexual relationships with patients have been considered unethical since Hippocrates, the broadening of the ethical prohibition about sexual relationships between doctors and former patients with the more recent addition to the APA ethics code (1), which states that a sexual involvement with a former patient is "almost always" unethical, has both clarified and left some ambiguity because of the language. The recent article by Dr. Paul Appelbaum and Linda Jorgenson (2) brought into clearer view some possible areas of ambiguity related to sexual contact after termination. While the APA Ethics Committee saw some possible usefulness in legal settings for an arbitrary time period after which sexual involvement might be permissible, the committee strongly disagreed with the conclusions from an ethical point of view.

A patient enters a therapeutic relationship with a conscious assumption about the doctor-patient covenant, as described by Webb (3). The patient assumes that the doctor will do what is in the patient's best interest, will not harm or will prevent harm to the patient, will not exploit the patient for his or her needs, and will allow the patient as much autonomy as possible. Before entering treatment the patient does not understand or appreciate the presence of unconscious wishes, nor does the doctor understand early on or at times during treatment the nature of his or her countertransference. Although all psychiatrists may not subscribe to this theoretical way of thinking, we can all fundamentally agree on some primary ethical principles that underlie ethical behavior. These include autonomy, beneficence, justice, and honesty. When there is conflict among these principles, as is present when undertaking an ethical analysis of sexual relationships with former patients, a decision must be made in favor of one or another ethical principle if all principles involved cannot be resolved. This is the dilemma in the proposal for an arbitrary time period after termination of treatment for the initiation of a sexual relationship.

Over the past decade APA has suspended or expelled over 113 members, most often for sexual exploitation. Without exception, when complaints of this type have been investigated and the psychiatrist involved admitted to the relationship, there have been no situations in which the relationship was considered ethical, no matter how long after termination of treatment it had begun. Although in the majority of cases the relationship began during or soon after termination, there have been several cases in which the relationship began 1 to several years after termination. These cases demonstrated harm to the "former patient," as judged by the investigation. Appelbaum and Jorgenson report that at the Minneapolis Walk-In Counseling Center, there were about 2,100 cases of therapist-patient sexual contact, with less than 1% in which sexual contact began more than 1 year after termination. A review of that information, however, with Mr. Schoener, who provided the data, indicates that of that small percentage, there were at least some cases in which harm to the patient was documented (G.R. Schoener, December 1991).

To prevent harm can we scientifically differentiate more and less vulnerable patients or those more or less vulnerable because of intensity or duration of treatment?

I think not. Some patients with ostensibly low vulnerability have been harmed. Some patients with low-intensity or very brief treatment can nevertheless harbor incredibly strong conscious, as well as unconscious, feelings or fantasies toward the doctor; these feelings or fantasies can be exploited without the patient's conscious awareness, also resulting in harm. Unfortunately, we do not have a scientifically controlled study with all variables considered, but we do have the collective experience of over 40 years of APA Ethics Committee complaint investigations.

What about patient autonomy? Could there be some patients who enter into a sexual relationship with a psychiatrist with true autonomy (without coercion or manipulation)? The answer is, theoretically, yes. Unfortunately, we have little to rely on other than anecdotal reports of happy marriages or relationships. We have not been able to systematically study those situations, since they are not the subject of complaints or they are community or collegial secrets. Whether these anecdotal reports have an ongoing, potentially detrimental ethical effect by creating an acceptable or rationalized role model needs further exploration.

One ethical dilemma, then, is balancing patient autonomy against potential or actual harm. It is here that the prevention of harm to current or future patients outweighs patient autonomy based on our actual experience.

Is it just to strongly side on prevention of harm to a few patients when there may be individual exceptions? Again, if we hamper one relationship that is an exception, we can be fairly certain that the psychiatrist and former patient can find relationships elsewhere. The harmed patient, however, may never again be able to trust in a reparative therapeutic relationship. Therefore, there is some argument for justice over autonomy in the strong prohibition.

Another ethical problem is balancing beneficence and honesty. If there were an arbitrary time period, patients would have to be informed of this possibility before the beginning of treatment. While wanting to do good and prevent harm, we would need to explain that we know that some patients who enter into relationships after 1 year *are* harmed. We would also need to inform the patient if, in our individual case, we would be open to the possibility of a relationship with the safeguards outlined by Appelbaum and Jorgenson. To imagine this discussion borders on the ludicrous, and it would seriously impair any psychodynamic therapy and might well impair other modalities of medical psychotherapy as well (although possibly in more unspoken or unexplored ways). In other words, it would be very difficult, if not impossible, to be completely honest without interfering in harmful ways in the psychotherapeutic process.

A further ethical problem would ensue by setting up a prospective experiment to determine whether an arbitrary time limit makes sense scientifically and ethically. Since we know that some patients have been harmed even after a longer period of noncontact, and without an adequate way to measure "real terminations" or whether transference really diminishes enough to ensure autonomy, this seems particularly hazardous to those experimental patients. We are interested in hearing from our colleagues who have had relationships with former patients and believe there was no ethical problem. While we can understand that the privacy of these situations may cause some reluctance to disclose them, this would at least provide some information (although retrospectively) and would not create or support another possible group of harmed patients through an experiment. We are also interested in hearing from patients who do not feel that they were harmed after a sexual relationship with their psychiatrist following termination. A comprehensive clinical interview by psychiatrists well trained in this area of ethics could help us to understand if there are many exceptions to the very restrictive ethical position and would permit an ongoing, although not strictly scientific, exploration into this discussion.

There is a further ethical duty to the integrity of the profession. With our current knowledge of possible patient harm and the necessity of the public's trust in the profession as a whole, we must resolve the dilemma in favor of the "almost always" position without any arbitrary time period.

The ethics of APA "are not laws but standards of conduct which define the essentials of honorable behavior for the physician." The foreword to *Principles of Medical Ethics With Annotations Especially Applicable to Psychiatry* (1) states, "The annotations are not designed as absolutes and will be revised from time to time so as to

be applicable to current practice and problems." As in all ethics complaints, under our procedures a member accused of any unethical behavior has the right before a panel of peers to argue why in his or her particular case the behavior was not unethical. The multiple levels of review provided give the accused psychiatrist ample opportunity to defend his or her position up to the appeals process. It is this peer process that is the final feedback to a member about how any behavior might be judged.

After this ethical analysis, however, we are left with the point raised by Appelbaum and Jorgenson that a more precise definition of the ethical standard might serve to protect rather than to harm patients. This is where we all agree. Where we part ways, however, is the means to that end. The "almost always" position has achieved some of the protection we wanted.

Should the annotations be clarified by the more definitive position that "sexual relationships with current or former patients are unethical"? For many of the arguments delineated here, my opinion and the opinion of many of us would be yes, again, with the understanding that the annotations are not absolutes and there may be exceptions both theoretically and actually. This suggestion should engender lively debate, as it will.

The APA Ethics Committee, the Board of Trustees, and the Assembly have all agreed that members are bound by our ethics as published. Current and future patients must be able to trust that their psychiatrist's dedication is solely for their welfare in order for treatment to succeed, and an arbitrary time period would weaken that trust. APA members must be able to trust that their Association's ethics annotations and procedures are fair in order to accept them. The real meaning of the current "almost always" position from an ethical point of view ought to be so strong that a proscription against sexual contact with current or former patients should presumptively be accepted when a psychiatrist becomes a member of APA.

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The Search: Body, Mind, and Human Purpose

Daniel X. Freedman, M.D.

Psychiatry's appropriate agenda and severe distractions in sustaining it are presently a concern and have historically been so as we struggle with the issues of linking body, mind, and human purpose. Biology requires behaving, variability, and the development of regulations to implement "purpose" in coping with the milieu. Psychiatry begins and ends with our patients—with their diseases and dysfunctions, their biographies and aspirations—which, as a clinical medical science, we must systematically study. Doing that, we will borrow from and pose problems for all the life sciences. New knowledge about how cells and biological systems acquire, code, and exchange information challenges all of medicine. In assessing our advances and future, we consider the history of biological issues in psychiatry and the "sins" of biologism or reductionism. We will see that research questions and strategies in the current study of disease and therapeutics have not fundamentally shifted from Freud and Meyer to modern molecular neurobiology. The tension between the socially conditioned purposive self and impersonal biological processes is an inescapable intrinsic tension for psychiatry of which we must be cognizant as we continue the search.

(Am J Psychiatry 1992; 149:858-866)

In his 1928 APA Presidential address, Adolph Meyer looked back at his 35 years in American psychiatry in order to look ahead (1). His underlying topic was psychiatry's search for an appropriate agenda and distractions in sustaining it. Sixty-three years later, I echo that theme. Arriving from Switzerland as a pathologist, Meyer found psychiatry to be largely "an institutional and legal task." He scolded himself for his dila-

tory discovery of the heart of the matter—the person who is the patient. That, he decided, is where psychiatry and its evidentiary base begins and is its final test. That is the Meyerian integrating idea of professional purpose—the benchmark that can readily elude us absorbed in the pace of progress (or by today's "mismanaged" care). Meyer referred to the "narrowing mind-shy and man-shy" mechanistic philosophy of the nineteenth century as obstructing his vision. Rather than preoccupation with the elements, he sought an integrative and adaptive emphasis on how the behaving parts, when put together, function throughout human life.

As a biologist, he would have agreed with Pascal, who had asked, "If nature is first habit, why is not habit second nature?" Biology, for all its wondrous mechanisms, means adaptive behaving and, inescapably—in the human—mentation. So both biology and mind mattered when Meyer focused on objectifiable behaviors, on habit and personality patterns. Further, he would concur with the emerging dynamic physiological thought (epitomized by Claude Bernard), which Freud and many contemporaries in their own ways shared.

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Of intrinsic necessity, many words and ideas in this article have appeared in one form or another in the self-citations noted. My purpose was to assemble my current views on the topics selected rather than to stake out territories of original data or thought. I am thus indebted to 50 years of experience with our field, to previous Meyer lecturers, and to colleagues, past and present, who in person or in their writings helped and continue to foster my education.

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Thus, developmentally we acquire and structure internal patternings—dynamic stabilizing *and* adaptive regulations—both biological and behavioral. And so for Meyer the term “psychobiological” meant that mental activities integrate and express both our human aims and bodily needs.

One sees him as resisting categorizations, theory, and dogma in favor of tested, carefully chronicled observations. As to our rush to fashion (which seems to me to be a kind of “intellectual ejaculatio praecox”), Meyer repeatedly warned of wishful illusions, of too concrete a belief in our imaginative “stories.” I refer to metapsychology and metapharmacology or “speculative neurobiology,” which, at their very best, provide tentative working hypotheses for but a part of the problems addressed. Meyer’s targets were mechanistic or theoretical preoccupations that omit human strivings. He called this “psychiatry without psychiatry.” As to defining psychiatry he remarked, “I sometimes feel Einstein has to deal with very simple facts as compared to the complex and erratic performance of the human—the happiness and efficiency of which we psychiatrists are concerned” (1). Happiness and efficiency are surely a broad intellectual mandate, but, for Meyer, the patient was the anchor. In sum, Meyer advocated attention to the personal and contextual details of illnesses and an unprejudiced openness to the “facts that count” (a phrase that he repeatedly used). His sermon applies to more than the 1,302 APA members in 1928. Thus, finding and holding the center is, I believe, psychiatry’s intrinsic problem, and we might wonder why.

PSYCHIATRY’S MULTIPLE PERSONALITIES: 1844–2000

First, looking briefly back with all that in mind, we can chronicle organized psychiatry’s journeys through its various incarnations. In 1844 we were convened as the Association of Medical Superintendents of American Institutions of the Insane (14 met in Philadelphia) and the *American Journal of Insanity* was begun; disease was seen as a brain or moral flaw, and a caring asylum practice was ascendant. In 1892 there was a change of name to the American Medico-Psychological Association; and even with this broadened interest when Meyer joined, there were only 245 members.

For academic psychiatry, 1910 was a critical date. For Meyer then built a multidisciplinary research faculty and designed a curriculum at Johns Hopkins University leading a slow trend to today’s university-based psychiatry. “Psychopathic hospitals” and research (some of which Meyer actively helped) were fostered in Boston, Colorado, Iowa, Michigan, and New York State following the models of the Worcester State Hospital and McLean Hospital. Academically led services and research were Meyer’s lifelong pursuit. He also actively encouraged the emerging lay and paraprofessional involvements. He welcomed Freud, taught with the father of behaviorism, Watson, and spent a brief sabbatical with Kraepelin. In essence, he said of all, “I

was not swayed into any idolatry” (1), and he sharply critiqued the explanation of everything by one theory.

The prewar developments that he encouraged, the mental hygiene and child guidance movements, were influential. Walter Cannon in 1915 had provided a psychophysiology for fight and flight. Psychological factors, perceptions, could thus influence both mental and physical pathology, and the psychosomatics of Graves’ disease was soon a lively topic. The psychiatric team’s accessibility and promptness in their wartime interventions with disturbed soldiers were applauded. Thus, in 1921, with 1,001 members, the American Psychiatric Association became our new name, while our 77-year-old journal became the now familiar *American Journal of Psychiatry*.

But a surge of postwar optimism and the contagious hope of prevention were prevalent. Meyer decried the shift from “the outspoken psychoses to . . . supposedly preventive activity and reformed family and sex life . . . material that is difficult to control and evaluate” (1). He observed in 1928 that “popular psychoanalytic propaganda caused a decided shift . . . when genuine psychiatric research had just barely begun” (1). These diversions were strikingly dominant by 1932 (2), but the community-based, psychiatrist-led teams (with psychologists, social workers, and various lay counselors) in clinics that psychiatry and generous mental hygiene fellowships recruited turned competitive. Along with neurologists and endocrinologists, team members engaged in private “mental health” practices. Of a later similar era (3), I noted (turning to the Bible for help) that we gave away our mess of pottage—and ended with a mess!

Community support collapsed in a backlash to excessive promises. Psychiatry in the 1930s also reacted by “remedicalizing.” Between 1932 and 1940 new organic treatments were begun (pentylentetrazol [Metrazol], CO₂, insulin, ECT in 1938, and lobotomies); psychoanalytic training required an M.D.; and specialty boards were instituted—all a counterweight to competition. And in World War II, psychiatry finally became a division equal to surgery and other medical specialties in the military and again received public plaudits. The National Institute of Mental Health (the second institute of the National Institutes of Health) was authorized in 1946, and after 1952 psychiatry was required in the curriculum of all medical schools.

Sanctioned by a new postwar surge of optimism, the 50-minute hour then became ascendant. Its simplest allure was the Freudian tenet that things may not be what they seem, and inquiries into the vicissitudes of self might unlock secrets or provide meaning. It thus engaged doctor and patient on a scale and scope as never before and surely had its excesses. But in spotting the tricks the mind can play when avoidance is at work, in exploring the gap between stated intent and actual performance, and in tracking the persistence of early wish and learning and patterns of expectations during dependency (transference), it provided a legacy for a canier dealing with human behavior (4).

And, as empathic insight and "hype" worked their way through the 1960s, the tonic of optimism was not only old wine in new bottles but in plastic, biodegradable ones! The psychiatrist-led team that had been reborn in the Veterans Administration and general hospitals of the 1950s peaked with the community mental health centers, where a new orgy of "professional role transvestism" (2) began! The escape from disease escalated. The secondary consequences of being ill—"labeling"—were construed as the real issue. The emphasis was on a civil right to be crazy rather than the tragic functional incapacity *not* to be.

But the psychopharmacological therapies were quietly emerging from the 1950s (when APA expanded to 10,000 members). By the 1970s, pharmacotherapeutics loomed as dominant, sparking the purely practical need to reattend to nosology. Biological psychiatry (the term to me is a redundancy) emerged from the mid 1960s and, with new lay support for it, dominated the 1980s. But that decade was more than the old wine of medicalization given the wealth of new and telling biological and clinical facts that count!

And so we come to the twenty-first century. While the competitors of earlier times in fact have truly burgeoned, APA's membership will soon be over 40,000. The 1990s, at least, have been officially—literally *Presidentially*—declared The Decade of the Brain (an appallingly short time if we truly ponder the challenge). Will brain science replace psychiatry? Will yet another professional personality and name change be in the offing? Perhaps the American Association of Brain Sciences? But experts in acronymic acrobatics might do better than the AABS!

PSYCHIATRY'S CENTRAL AGENDA

Now, whether all this to and fro is a part of the natural tides of history and simply a response to evolving discovery and socioeconomic necessities is difficult to determine. Amnesias about intrinsic purpose, about what we serve for, recur in all collectivities chartered for special societal services—the church, the law, the university, or medicine. But psychiatry has a special fuel for some of these oscillations.

Thus, for our forefathers as for us, the core issue is no more or less than the nature of human nature. Psychiatry, then, intrinsically embraces both broad concerns and their pragmatically narrower derivatives, since we deal with impairments in the very psychobiological tools with which humans attend to, express, and effect their personal purposes.

More precisely, there is an underlying complex question actuating psychiatric thought—how mind and body are linked. For we ask how it is that living matter can accommodate the links of bodily function, subjective experience, and overt behavior (5). The search for how the living organism can gain organization and self-possession, let alone generate the perception of an "I" implementing purpose, enlists a wide range of parties

from the humanities to developmental psychobiology. And in the mind of every child and educated adult the image of the causal "I," the mover of events, is variably expressed (6). Questions of mind and body, though embarrassing, cannot be ruled away; they are intrinsic to human thought and recurring and sometimes practical in our work. Thus, for psychiatry, both breadth and focus will inevitably comprise an intrinsic dialectic and tension. Of that fact we must simply take charge.

At a more practical level, we are, as I politely tried to put it (7), concerned both for the "distress of the healthy and the health of the ill"—or, in English, with both mental health and illnesses. We are concerned with normality and pathology, individual dynamics and families, psychosocial processes and molecular sciences, and much more. How, then, do we concretely define our professional purpose and scientific agenda?

Some call us a behavioral science. Some of us rush to be exclusively biological, psychosocial, or psychodynamic and to wear our identity badges. But taking an inventory of this breadth, in cataloging all this as well as our concern with the mind, one does not have a core definition of our function. There is, in brief, an invitation to pretentiousness when we forget what Meyer stressed: psychiatry as one of medicine's progeny deals with the disturbed function and biography of the person who is the patient.

So in our breadth and our borrowings, our defining intellectual business is the study of disease and dysfunction. Thus I have come to define psychiatry as one of medicine's clinical sciences, a part of the family of the life sciences (8, 9). Every clinical science must aggregate and assess the state of the art and knowledge bearing on its diseases. That has never been the prime agenda of the essential contributory disciplines including what is now called the neurosciences. It is, further, an escapist illusion to believe that other disciplines contain and hoard secret treasures that, if we only knocked on the door, would unlock the answers needed for relief of human suffering (9).

When a new perspective or technology or concept is needed, we will, do, and should cross many interdisciplinary bridges, but always with a question in mind and not with the naive hope of rescue (8, 9). Psychiatrists themselves range into fascinating areas—genetics, molecular neurobiology, cultural anthropology, brain imaging, and more. But we cannot all board fleet monorails winging to the future or pursue ivory tower interests, leaving unattended the core issues. Thus, at the heart of the matter, we must study disease and dysfunction.

That study spans the parameters of etiopathology, predisposition, and precipitating factors and seeks the determinants of symptom expression and its cascading consequences. The job of studying the course and outcome of disease is taxing. The critical search for pathophysiology—or the mediating mechanisms—is in its promising infancy but demanding. It requires study of compensatory adaptations to internal psychic barriers, to impaired bioregulatory systems, to conflict-gen-

erating social signals and internal urges—all of which are ultimately manifest as the signs and symptoms of disease. The study of all this, in addition to therapeutics, their mechanisms and efficiency, and systems of care to enhance optimal function, should keep us busy enough.

Finally, the clinical sciences in practice use what I call the clinical process to investigate the individual patient. It has much in common with the logic of investigative research. It is a highly disciplined and sustained process of both personal commitment and investigatory skill and logic. It is a privileged engagement in enhancing human purpose. It is the essence of the medical model (3, 8, 9).

So, if the study and treatment of dysfunction and disease is our mission, how far have we really come, how did we get here, and how should we think about it? Sketching a perspective on that, I hope simply to share a view that provides me with some framework with which to encounter the alluring future as the search goes on. I will thus touch on where we are on etiology, then in therapeutics, and our research strategies. Finally, I sketch some thoughts on our attitudes about human biology in search of human purpose.

ETIOLOGY AND PATHOPHYSIOLOGY IN PERSPECTIVE

In our searches we now face an enticing, not altogether unproductive, new distraction as molecular biology becomes vividly alive in a way our forefathers could barely imagine. In all of medicine, for the bedazzled clinician the sweep and promise of modern science is, in fact, breathtaking. We should be appreciative but not mesmerized. For, in sobriety we will have to determine which of the plethora of science leads to apply practically in the clinic and clinical research. The gap between visions of what may be and application is still huge but narrowing.

Thus, we are witnessing the second revolution of molecular biology, mapping the human genome and tracking which among millions of proteins are key to a myriad of brain mechanisms and cellular regulatory processes—and which, in the service of gene expression, are responsive to signals transduced from the environment. We are now disarticulating the membrane-embedded amine receptors, precisely tracking their genealogy to particular DNA segments. We are deducing the codes of a profusion of Rosetta stones to understand how intracellular, intercellular, and organismic communications are governed as the various neuronal aggregates go about their massively predetermined—yet conditionable—business. The patterning of nature's designs is clearer. From all this and more, if we stick in our thumb we will pull out some plums. But we still have chores ahead.

In psychiatry, taking advantage of what *is* feasible, we should be pleased. We compute electrical signals from human brain and now deduce the regional brain patterns relevant to function or certain patterns of in-

formation processing, and we are imaging the functioning brain. We are diagraming hitherto unimagined cellular transactions induced by drugs and have quasi-receptor-specific drugs to change and probe brain processes as well as to treat. Measuring hormonal and behavioral responses to such probes, we deduce otherwise inaccessible events. Indispensable are the psychometric tools and precise clinical research designs to objectify our treatments and diseases, and we design operationalized manuals for psychotherapies. With positron emission tomography (PET) (10) and magnetic resonance imaging (MRI) (11) we track postnatal brain development over the life cycle, discerning patterns possibly relevant to schizophrenia. We now witness real momentum. In brief, if you have to be ill (and we now soundly know that some of us do), one is far better off being so today than 50 years ago when I first encountered the field.

In perspective, the past held its own wonders. One can imagine the confidence that ECT generated, and we can intuit the sheer gratification in establishing the etiology and prevention of psychiatry's "two Ps," pellagra and paresis. So, in historical glimpses with perspective as the aim, my purpose is not the detail but to grasp the rate of change and the way things are and go with science.

For the paresis story we had to begin by plucking it out of a welter of psychoses. Thus, descriptive psychiatry gained in precision while groping off the mark for cause (dissolute character, "libidinal excess"). The rest of the story illustrates a characteristically long and indirect journey: in 1904 to neuronal pathology (by Kraepelin's colleague, Alzheimer), in 1906 to a quasi-specific Wassermann blood test for disease detection, to identification (by Noguchi and Moore) of the pathogen in brain in 1910, and then in World War I to specific therapeutics. The spirochete was, in effect, finally burned from the brain by Wagner-Jauregg (the only psychiatrist to receive a Nobel Prize) with his fever therapy. Penicillin—one *war later*—then specifically targeted the bug. Yet after that journey (almost too logical compared to others in medicine) we still do not know the exact pathophysiology leading to the characteristic mental symptoms.

For the pellagra story clinical description was simple. Research begins with epidemiology—Joseph Goldberger's tracking in 1914 of the affected in institutions implicating diet (patients but not staff had pellagra). This upset the consensus of two U.S. commissions of an infectious etiology. Rather than poverty per se (also tagged as "causal"), specific dietary elements (eggs, protein, and so forth) were key. Research and therapeutic maneuvers preceded the precise science solution but also punctured some causal myths. Goldberger persistently searched (12) in bold human experimentation (injecting himself with fluids from patients, manipulating diets both to produce and cure pellagra). With an animal model, he generated a specific hypothesis of an amino acid and vitamin deficiency, which, long after his death in 1929, was verified when, in 1937, nicotinic acid was

identified (and the role of dietary tryptophan later clarified as its endogenous precursor). Yet the exact pathophysiology by which but *one* of the various B vitamins leads to such specific symptoms is still unknown.

These two triumphs are the simplest problems among our many diseases. For all the rest, our powerful science has not yet unearthed the causes of, or precise predispositions to, the pathogenic initial disequilibria and the cascade of consequences we recognize as symptomatic disease. Thus, with all our power, we have promises yet to deliver and miles yet to go.

The pharmacotherapies compelled belief that brain chemistry is relevant, either to etiology or at least to repair. We search—but to date there is no clear proof that etiology is so linked. There is ample proof that dysfunction can be *compensated* for, although not necessarily repaired by, drugs. Thus, for all our power to understand synaptic regulations, we are still calibrating precisely where and how brain substances and mechanisms are relevant to the manifestations of disease. We want to know whether brain receptors are different in the diseased patient—as they ought to be. We have truly enticing starts, some secondary pathophysiology, and a high index of suspicion as to genetics, but to be clear: *clinical diagnostically* specific, etiopathological definitions of our diseases remain an ultimate goal.

THERAPEUTICS IN PERSPECTIVE

To telegraphically compress the sweep of the history of therapeutics, I emphasize two points. The first is that over a century ago we were using combined “moral” or supportive therapies and any available somatic therapy that held allure. With refinements in psychosocial and drug treatments, this is still the case. Second, our *current* pharmacotherapeutic armamentarium derives largely from the postwar period to 1966. In the subsequent 25 years, our recent past, we have mainly been fine tuning what we long had in hand. The correct lower neuroleptic dosage range is now being calibrated. There are new uses of old drugs—carbamazepine for mania, monoamine oxidase inhibitors for panic disorder and more, massive thyroxine for rapid cyclers, and other examples. Clozapine and novel antidepressants are not “new” but simply at long last available.

We now search beyond acute treatment for secondary prevention—the prevention of relapse. Brilliant research from the Western Psychiatric Institute and Clinic of the University of Pittsburgh clarifies that recurrent unipolar depression is far more frequent than we have grasped. Changing the sound conventional wisdom that “lower drug dosage and duration is prudent,” researchers find that *sustained* and *high* doses of imipramine are strikingly effective for prevention of relapse over a 3- or 4-year period. Further, specific psychotherapy (interpersonal therapy) enhances the drug effect and, while less potent on its own, has demonstrable efficacy (13).

Perhaps the most unanticipated recent discovery is

the *selective* utility of serotonergic drug therapies—not only for obsessive-compulsive disorder (for which cognitive behavior therapies are useful), but even for peculiar compelled behaviors such as trichotillomania. Now all this is the mark of a thriving and inquiring clinical discipline systematically at work in serving the ill with greater skill. Nevertheless, we have nothing approaching the etiopathological specificity of our two *Ps* in hand. Nor do we have therapeutic specificity. We do not have drugs that are solely antischizophrenic or exclusively specific for only one of the various *DSM-III* disorders. Our treatments are, at best, symptomatic.

Looking ahead, we want predictors to permit a match of therapies for the individual patient. We will design molecules to reduce or treat side effects. The *targets* of drug research may well shift. Beyond axis I diagnoses, we will be looking at particular drug-reactive components of behavior or disease, not unlike the serotonin-mediated dimension of reactivity or diminished impulse control. Negative and positive symptoms of schizophrenia will be approached on the basis of excitatory amino acids and the newer neurocircuitry of glutamate-mediated cortical loops to subcortical gating and filter systems. The number of tools and growing understanding of their targets strikingly improve the odds of serendipitously winning at this roulette.

Yet while we can hope for specificity, we simply do not know if we should. For we do *not* have a fundamental grasp of the limits and costs imposed by the varied ways by which these interconnected brain organizations and their receptor systems work, adapt, and respond. This is fundamental and critical. In brief, in manipulating brain regulatory systems, we do not know how far we can legitimately expect to go.

We unarguably have a variety of drug and behavioral therapeutic options in hand. The reason may not only be ignorance. Rather, it may derive from the way physiologic regulators work and how, in the abundant redundancies of nature, the brain is built to seek and use a variety of significant inputs. Normally, the most effective way to talk to the entire complex of our receptor- and membrane-linked systems is through the symbols and signals that the psychosocial sciences study and that interpersonal transactions comprise (8). How the brain codes and reads those signals is still unclear. It is, however, clear that psychiatric disorder may require new learning or—what is often now undeniable—molecular stabilization of vulnerable mechanisms. Most probably, both are most often needed.

Fundamentally, what we really seek in the way of pharmacologic contributions is to use nature's logic and gain as much drug specificity as the intrinsic system will allow. This logic allows hypothesis testing to tease apart and reveal mechanisms and their links to the “anatomy and physiology” of behaviors and symptoms. Both drugs and endogenous agents (like the endorphins) act as ligands binding at receptors. Accordingly, we will improve on nature and manufacture what I call “ligandomimetics,” based on such logic. Further, in the far future, we will understand exactly what the

products of specific genes are and use them therapeutically. But to decode the myriad of interactions and define the modalities and dimensions through which gene products influence observable behaviors is not yet fully accomplished for even simple nervous systems, neither for Kandel's snails (we do not yet *quite* have an "ego for the escargot"), nor even for single-cell organisms that, as we do, move, approach, and avoid with something like memory as a guide. It makes one wonder if directionality in simple systems is somehow a precursor of intentionality in the human. We do not know.

RESEARCH STRATEGIES IN PERSPECTIVE

So our research proceeds with what is doable, and we race to catch up with what might be. As pleased as we are with these visions, we ought not be too contemptuous of the past. Our forefathers were not dumber than we. They simply were not as well equipped with information. By 1949 life stress and bodily disease was a hot topic. Long-loop feedbacks from brain to the adrenal and back were seen as regulatory well before the short-loop presynaptic and postsynaptic feedbacks were discovered in the 1960s. Work, eventually garnering Nobels, had *already* begun on the prohormones that are now center stage. Corticotropin-releasing hormone is an example. The brain even then was seen as an endocrine-generating and endocrine-responsive organ.

Strategies in hand long before chlorpromazine are quite similar to ours (appendix 1). To pick one central example (point 2), energy hypotheses are now directly studied with PET scans. Claude Bernard actually laid out the basic groundwork for PET and did so in APA's journal, startlingly in 1872 (14) (and also "innocently" observed conditioned responses that Pavlov would rediscover and systematize). Some of the treatments testing energy notions were bizarre, but the underlying thought that linked metabolism and function was not. The biology of the mental patient was inefficient. Mental disease was not a failure of will, but somehow of the energy to be able to deploy attention at will and to stay sturdily and responsively in touch with the environment. Meyer himself characterized his "response dispositions" as "ergasias"—a neologism that captures the sense of momentum and work intrinsic to adaptive performances. Point 4 refers to the search for special biological stigmata to identify disease. We do not yet have the convenient biological markers either specifically to tag a disorder or trace genetically-linked disorders in the pedigrees of our patients, although eye tracking—elegantly identified *before* World War I (15)—is now being so applied in the schizophrenias.

We thus seem to have come far but, perhaps, not as far as our excitement implies. The old research strategies persist. What is biological about psychiatry is not determined by what we measure, nor how we treat, but rather by how we think about what we discover and do (9). In that vein, the clear concept in 1950 was that external or internal signals will activate normally synchro-

nized behavioral and bodily systems and that mental disorders are reflected in some sign of their dysregulation. If there were characteristic differences at steady state, or with challenge, a deviation would provide a lead. Thus, Bernard and others generating nineteenth-century physiologic regulatory theory still underwrite our current momentum.

BIOLOGY AND HUMAN PURPOSE: THE SEARCH

For the last lap of this race, I want to address problems in our attitudes on biology in the search of human purpose. To render specificity to all this, recall that our forefathers sought a brain that could account for behavior, as we now do. I have called the pre-1940 picture of brain "Prometheus Bound"—a switchboard's inflexibility. Discoveries in the 1940s changed that, but the key notion is that the brain is preponderantly built to behave; it is inexorably generating response, "behaving," so to speak, an instant before we can see a behavior. And even if injured, the components are constantly operating. In fact, manic-depressive disease persists after hemispherectomy, and we see drug-responsive vegetative depression after extensive brain damage. No wonder the task of extracting or controlling key mechanisms or finding disease-specific ones is complicated, since the prior state of these ongoing but incompletely defined neuronal operations largely determines the fate of the next input. So we now indeed have a responsive brain but also a set of complexly connected moving targets. This surely complicates deductions of biobehavioral mechanisms with our simple experimental controls. Very basic biobehavioral operations—vigilance, arousal, habituation, sensitization, startle—and more complex ones (e.g., attention, affect, memory) are still not sufficiently dissected for precision in linking brain and behavior.

In a lecture, the title of which has the hubris to refer to human purpose or intentionality, I might as well plunge, dive deep, and speak of the hunt—not for the Red October, but for the commanding and causal "I." As far as I can tell, in all of neurobiology, the hunt has never produced a capture. With Pennfield's depth electrodes in humans, the deciding or decision-making event was not to be found. In recording evoked potentials, the fact of a decision—but not the making of it—is detected. We find the effect but not the command.

What, then, about the juices of the brain—the monoamines? What do *they* signal and control? Now as to the game of what the amines mean, I have spent a professional lifetime either watching it from the bleachers or episodically working on the field. Yet if I closely watch a patient, I cannot normally tell whether the amine levels are up, down, or in between. Of course, there is parkinsonism. But a dopamine depletion of 70% is necessary for symptoms to be visible. Given the right challenge paradigm, we might someday detect, before the clinical fact, that something is amiss. But note that the amine deficit or neuroleptic dopamine block-

FIGURE 1. E. Power Biggs Makes the Music!



BUT: Don't Confuse Peptides or Amines With Music

ade does not force the parkinsonian behavior. Rather, in the absence of dopamine, the ongoing and busy (and multitransmitter-regulated) striatopallidal activity emerges. In the nineteenth century, Hughlings Jackson described precisely this emergence of unchecked lower systems when the brakes are off. One wonders when neural or psychobiological regulators fail whether this in turn "taxes" amine systems to compensate. If so, keen phenomenologic diagnosis does not answer the question.

For our purposes, the question is, what do the amines mean? Do they make something happen? I speak to the point of command or direction. Thus, in the cartoon (figure 1), E. Power Biggs (the superb Yale-based organist whose recordings of Bach from the 1940s on are still valued) strikes the notes and we hear the music. What is going on in the mechanics of the grand console that produces the precision he intends is not visible. To extend this analogy, we cannot confuse the peptides and amine transmitters with the music that E. Power Biggs intends and commands. Assume that the various organ keys are specific drugs and that we therapists were as skilled as Biggs. When we strike the various drug keys we unfortunately will have lost precision. And that is because we let loose a flurry of mediators of

ongoing self-regulating systems. Neither we nor amines command specific behaviors. There, indeed, is a high specificity of the targets of amines, but their effects on biobehavioral operations are modulatory. Their effects are often state dependent. Put an electrode in the hippocampus (as Segal and Bloom did) where norepinephrine mediates the target cells. Now sound an auditory signal, and the effect of added norepinephrine on the hippocampus is inhibitory. Then give the signal value (implying food to come), and the effect now enhances facilitation (16).

The link of LSD to serotonin, where I began in the 1950s, neatly shows such modulatory effects. Serotonin itself is not psychotomimetic. LSD, we find, acts at various serotonin receptor sites, but as an "imposter" (17, 18). It sends signals from the postsynaptic receptor telling other systems there is too much serotonin when, in fact, the drug actually *reduces* serotonin in the synaptic cleft (acting at a nerve-ending autoreceptor to prevent serotonin release). This "deception" miscues a number of interneuronal regulations. But, to our point on what amines do, certain increases of serotonin will buffer LSD effects. And, in rats, with only a 10% depletion of serotonin, four times *less* LSD than is normally required for a "trip" to be triggered now becomes potent. Thus, in general, a "dimension of intensity" (19) is affected by the amines, which are themselves servants, so to speak, of other ongoing processes.

We cannot, then, either in a specific neurone or brain juice find a precise locus to satisfy our convictions of an operative "I." What we interpret as that homunculus is surely the *product* of multiple regulatory equilibria that, in sum, produce deftly adaptive response. I know of no higher mathematics, computer models of intelligence (appendix 1, point 10), or measures yet in hand to compute and capture such high-level integration—and certainly none that direct one to confirmation through experimental studies of living brain.

Our interest in biological regulatory mechanisms is practically linked to behavior. But for this focus we are accused of the sin of "biological determinism." In fact, what is being determined are the limits, capacity, and flexibilities of the intrinsic organizations with which we as physicians must and do ultimately cope. For Bernard, determinism refers to the immediate or determining cause of phenomena. This "differs from fatalism, on which we cannot act . . . [With] search for the causes determining phenomena . . . materialism, spiritualism, inert matter and living matter cease to exist; only phenomena are left, whose conditions we must determine . . . Scientific determinism ceases here; there are only words beyond, which are of course necessary, but which may delude us if we are not constantly on guard against the traps which our minds perpetually set for themselves" (20).

We are also accused of "biologism." Biology is, in a sense, a nuisance; its workings should be so smooth as to permit one to ignore its mischiefs and, of course (given the boundlessness of pride and wish), the slightest hint of *intrinsic* constraints. Professionally, we can-

not ignore biology. I suspect that the underlying fear of critics derives from the concretism and certitude of our pseudoexplanations, the metapharmacologic vision of us, as a superprecise E. Power Biggs, at the grand console of behavior. But, in fact, biology means, indeed provides for, chance. Behavioral biology reminds us that DNA "expects" an environment and *absolutely requires* its cues. DNA's very structure, its blank areas, and self-replications provide for order but also for error, mutability, and chance from conception and forward to the end. We are thus built to behave and have some room to do so innovatively—for better or worse. The brain, like DNA, also has blank spaces and, of necessity, acquires memory and attitudes, constructing a history through time (8). Nature's instructional and expressive designs entail a ceaseless interplay of the seeking and the sought. In embryology we see a nerve seeking a target that signals an interest and in the human, a search for sources signaling nurturance (4, 9). This choreography of the dynamics of behavior in a varying environment is being discovered at every level. That is the design.

Both those uncomfortable with biology and those exaggerating its certitude might note the inexorability of chance and variation intrinsic to biology. Each organism is, in its expressed DNA repertoire, to an extent unique. That means no escape from dealing with disease variations. All biomedicine might forgo the notion of ultimate rigid control of outcome in the name of therapy or prevention. Biological systems, including the behavioral, do not work that way. Nature does not need the visions of omnipotence that console us, neither illusions of mastery nor of the lofty privilege of dismissing its designs (9). If we are biologically centered at the moment, it is not a matter of ideology but because new insights are now feasible. Psychotherapy research is increasingly systematic. Mental operations and relevant neurocircuitry may someday be saliently dissected with improved research tools and designs. Psychiatry from all this will lose neither its mind nor its brain—nor its essential function to search in any realm yielding to probing inquiry.

Another putative sin is that of reductionism. It *can* divert our attention from the person who is the patient or as to why we legitimately ask questions in the first place. But reductionism is also necessary to produce the leads to understand nature's logic. Genetic knowledge has been derived from such banal witnesses as garden peas, fruit flies, fossils, and bacteria. The psychiatrist who studies rats or chopped liver to search for an enzyme is not trying to "rodentomorphize" man nor memorialize mother's cooking (21). We are searching for designs. Our so-called reductionistic clinical pursuits (say, measuring hormones in patients) are pursued with a wealth of evidence that altered biochemistry and internal molecular regulations are reflected not only in cellular changes, but in changes in the integration and control of small or large components of an organ, the functions of which appear to create the links of mind and body (21). We thus are paradoxically condemned

to deal with highly responsive but ultimately totally impersonal biological processes when we assist our patients to find personal purpose (8).

Drugs, in their effects on attention, perception, affective, and cognitive operations, in fact are ultimately influencing rates and rhythms. The heart, one scientist noted, is composed of wires and juices, as is the brain. These regulate heart rate and rhythm and influence the force and efficiency of output. It is probably the same with the brain. We know our drugs are affecting stop and start mechanisms and their thresholds, which in turn change the rate and range of signals through which a nervous system operates (8, 22).

We should not be impatient. After all, we are only daring to decode the messages that multimillenia of evolutionary trial and error have produced. We inherit, as Paul MacLean reminded us in his 1982 Meyer lecture (23), a reptilian and mammalian brain as well as our unique enlarged frontal lobules—perhaps one-third of the distinctively human brain. And if that evolutionary design had intent, it surely can be and has been criticized for its awkward and archaic impositions on our wish and will! Our huge "dictionary of ignorance," in perspective, is thus not surprising. So we must calibrate our expectations as we piece together the various elements of the story. In medicine we usually have *partial* stories. It is a long and jagged trajectory. We cannot always require the eureka-like leap from the unknown to the definitive final answer, even from the current wonders in hand.

Is all this brain and biology psychiatry's business? My answer, of course, is yes. There are currently fantasies that some fictional all-embracing "clinical neuroscience" will totally replace psychiatry. This is another version of what I call "the game of the name." I do not believe that the lions and lambs of neurology, neurosurgery, psychiatry, and molecular neuroscience, peacefully grazing the pastures of brain together, usefully pictures what we must inevitably confront (4, 22). For it is the different *diseases* these clinical sciences are charged to comprehend that pose their *own* agenda of urgent puzzles and needed interventions and hence, the *sequence* of *particular* questions to be posed to the indifferent complexities of nature. The psychiatric patient—our benchmark—presents the problems to which someone must specifically (and comprehensively) attend. It has been noted (22) that if we abolish psychiatry, a race of "psychiatroids" would have to arise to replace us!

And so we search, knowing that every question answered in science generates new ones. When I arrived in California a few years ago, I did not want to consult astrologers and so consulted an old friend (a guru?). I said to Arthur Yuwiler, "We're poised 'twixt pride and perplexity. What will the fate of science be?" He answered: "There are many things we know for certain—but we don't know which are relevant; there are many things we know are relevant—but we don't know for certain what's going on." And that is the way it has been, is, and will be.

The tension between biology and the accurate perception of a socially conditioned but uniquely purposive self will continue. As all living species, we face impersonal forces that in part frame destiny as we seek and assist others in the quest for personal meaning and dignity in this brief transit (8). We cannot disregard nor be intimidated by nature. We can not make the rules for mind and body, nor precisely orchestrate its transactions. We can, however, search, as Meyer did, for "the facts that count." We can, in brief, search to understand "the way things are" rather than what we wish them to be. That is the *key* search. Of such search Bernard (20) noted, "True science suppresses nothing but goes on searching . . . undisturbed in looking straight at things it does not yet understand." The scientist never grasps truth in its wholeness, but rather "significant fragments; and these fragments of universal truth are precisely what constitute science." We are, he said, "never self satisfied, but still continue to strive . . . This is the feeling which Pascal expressed in somewhat paradoxical form, when he said: 'We are in search never of things but of the search for things.'"

Doing just that concretely positions us to know what may *really* be possible. With that in hand, we truly *can* focus on the person and saliently assist in Meyer's goal for psychiatry: to enhance the happiness *and* efficiency of those whose human strivings we are specially privileged to assist.

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APPENDIX 1. Research Strategies in Hand Before Chlorpromazine

1. Clinical epidemiology: retrospective, prospective, cross-sectional, and family studies; community "surveys."
2. Energy hypotheses: tests of O₂ and metabolic differences in brain and body.
3. "Models" and psychotoxins: "Is psychosis in the blood?"—make a "measurement search." Activate anxiety or psychosis (mescaline, LSD, stimulants, adrenergic drugs, CO₂).
4. Challenge tests: e.g., histamine and blood pressure in schizophrenia. If a function differs with challenge, then deviations (whether a cause or consequence) provide leads.
5. Hormonal links: hormonal diseases and mental symptoms.
6. Psychobiology of stress, arousal, attention: autonomic and hormonal response to probes: ergotropic and trophotropic imbalances, and so forth. (We still struggle with an old problem.)
7. Brain structure and function: deduced from EEG, neuropathology, pneumoencephalography (now: PET, MRI, and so forth).
8. Cortical-subcortical links: limbic systems, neurobehavioral studies with lesions, and so forth.
9. Theoretical "models" of a brain that can work: Freud, Sherrington, McCullough, Eccles, and others.
10. Concepts of biological "operations": physiologic regulatory theories (Claude Bernard), homeostasis and "hyperexis," cybernetics (information > energy) (now: computers and neural nets, artificial intelligence, chaos theory, "attraction states" or set points, oscillators, holograms, and so forth).

Mania in Late Life: Focus on Age at Onset

Robert C. Young, M.D., and Gerald L. Klerman, M.D.

The authors review current understanding of manic syndromes and bipolar disorders in the elderly, emphasizing the limited number of systematic studies available. Discussion is focused on the validity of late age at onset as a nosologic distinction in geriatric patients. This issue is contrasted with possible age-associated effects on early-onset illness. Data regarding incidence and prevalence in the elderly are assessed, and the high average age at onset of mania is noted. The review cites evidence that relatively low rates of familial affective disorder and increased frequency of certain diseases and drug use are associated with late age at onset. Aspects of psychopathology in the elderly, course of illness, and outcomes including chronicity, mortality, and cognitive impairment/dementia are considered. Management of these elderly patients is briefly discussed, highlighting questions concerning response to lithium salts.

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With the increased longevity of the population and the generally increased acceptance of psychiatric care, clinicians will see increasing numbers of manic elderly patients (1). These cases involve special problems for diagnosis and management. There are many important unresolved issues for research; these include characterization of the course and outcome of mania in the elderly.

In geriatric major depression, age at first onset of illness emerges as a heuristically useful distinction (2). This review focuses on the validity of this distinction for manic states and bipolar disorders in elderly patients. The distinction is contrasted with the effects of age on early-onset bipolar disorders.

DIAGNOSIS AND CLASSIFICATION

The Manic Syndrome

A considerable degree of international agreement has been reached concerning the complex of signs and symptoms that constitute the manic syndrome. Several sets of operational criteria for mania and for bipolar illness have been developed. In the United States, these include the criteria of Feighner et al. (3), the Research Diagnostic Criteria (4), and those of DSM-III and its

subsequent revision, DSM-III-R. They are similar to those of the World Health Organization's ICD-10.

Manic syndromes differ in severity. Traditional nomenclature has included at least a distinction between mild (hypomania) (5, 6) and more severe states. DSM-III-R includes three grades of severity. In DSM-III-R, manic states accompanied by delusions or other psychotic features, which are not necessary for the diagnosis, are distinguished from those without such features.

Diagnosis

Bipolar disorder. Most patients with manic syndromes have bipolar affective disorder. This is conceptualized as an idiopathic or functional disorder that meets the conventional requirements for a disease or illness (7).

Organic mood disorder. Some affective syndromes, including mania, may be considered symptomatic, i.e., etiologically linked to certain diseases and drugs (8, 9). In this context, Krauthammer and Klerman (9) used the term "secondary" in the sense in which it is used in general medicine. Such syndromes are an important issue in older patients in particular. In DSM-III-R, manic patients judged to have a disorder that is symptomatic, or secondary in this sense, are categorized as having organic mood disorder, manic.

Schizoaffective disorder. Manic signs and symptoms also characterize patients diagnosed as having schizoaffective disorder. This disorder appears to be related to bipolar illness (6). Schizoaffective disorder is not frequently diagnosed in the elderly.

Differential Diagnosis

In elderly patients, the differential diagnosis of manic syndrome includes paranoid schizophrenia and related disorders. It also includes dementia and delirium.

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TABLE 1. Types of Bipolar Disorder

Type	DSM-III-R Diagnosis	Characteristics	Comment
I	Bipolar disorder	Hospitalization for mania and major depressive episode	
II	Atypical bipolar disorder	Hypomania and major depressive episode	Can become type I with age
III	Cyclothymia	Frequent hypomanic and depressive symptoms	Can become type I or type II with age
IV	Organic mood disorder	Secondary to disease and drugs other than antidepressants	Cases unrelated to drugs of abuse may more often be of late onset
V	Major depressive episode	Family history of bipolar disorder	Can become type I or type II with age
VI	Bipolar disorder	Unipolar mania	Can become type I with age

Manic patients can experience grandiose and persecutory delusional ideation. Paranoid schizophrenic patients and patients with delusional disorders, on the other hand, can manifest excited, agitated behavior, and express grandiose delusional ideas. For such patients, however, obtaining a longitudinal history establishes the chronic nature of their psychotic mental content and the inconsistency of their affective features. In the past, manic patients with psychosis were often misdiagnosed as schizophrenic; for some elderly patients this diagnosis may have erroneously been carried forward.

Manic patients can present with cognitive dysfunction. Both dementia and delirium, on the other hand, may be associated with affective symptoms of a manic kind. These include restlessness, sleep disruption, irritability, lability of affect, and poor social judgment.

Classification of Bipolar Disorder

Subgroups of bipolar disorder based on course and family history have been proposed (6) (table 1). Type I represents patients hospitalized at least once for a manic episode, for whom there is also a history of major depressive episodes. Type II patients are those with both manic and depressive episodes, but the manic episodes have been mild (hypomania) and have not resulted in hospitalization. Type III patients are those with cyclothymic fluctuations in mood without major depression or mania. Type IV patients are those in whom the manic state is associated with illnesses or medications considered to play an etiologic role. Type V patients have histories of major depressive episodes alone but have family histories of bipolar disorder. Type VI patients have histories of mania but no depressive episodes (unipolar mania).

While chronology (3) has been useful as a classification system for major depression in populations of mixed ages, it has been used less for mania and bipolar disorder. In the aged these may be chronologically the

first diagnosable psychiatric syndromes, i.e., they may be "primary" according to the classification of Feighner et al. (3). Mania or bipolar disorder that is chronologically "secondary" (3) or "complicated" (10) has received even less attention in the elderly. Mania complicating a primary degenerative dementia is an example relevant to the elderly population.

Age at Onset

Manic states, like depressive syndromes, can occur throughout the life span. Age at the time of the first episode of illness must be taken into account in studying mania in the elderly, since widely differing longitudinal histories are noted in these patients (11-14). Elderly patients who present with mania may be experiencing the first affective episode, the first manic episode, or a recurrence of episodes that had their onset in young adulthood.

Patients with mania occurring for the first time late in life may or may not have had prior depressive episodes. If there is a history of depressive episodes, they may have been recurrent in early life. Affective illness thus can change polarity in late life. These patients may or may not have a family history of bipolar illness; if they do, they would have been categorized as type V bipolar patients early in life but become type I or type II in old age. The rate at which young adult type VI bipolar patients become type I with advanced age is also open to investigation.

Studies that have examined age at onset of bipolar disorder have differed in the definitions of "early" and "late." In samples of patients of mixed ages, the median age at onset has generally been used as the criterion. It is therefore difficult to relate findings from such studies to geriatric patients.

Krauthammer and Klerman (9) noted that relatively late age at onset (over 40 years in patients of mixed ages) was a characteristic of manic states associated with medical or neurological conditions or drugs. That is, type IV bipolar disorder, or organic mood disorder, manic, is associated with late age at onset.

EPIDEMIOLOGY

Overall, the rates for both the incidence and the prevalence of mania are apparently considerably lower than the rates for depression in the elderly, as they are in younger adults. However, there have been no large-scale community surveys of geriatric populations that would allow the development of accurate, age-adjusted incidence and prevalence rates for mania and/or bipolar disorder. The studies we have, particularly the National Institute of Mental Health (NIMH) Epidemiologic Catchment Area (ECA) study, have not yet reported on a sufficient number of elderly patients, although in some of the ECA communities, there was oversampling of the elderly (15). Also, the National Institute on Aging has undertaken some community epidemiologic surveys.

Birth cohort effects, reported in affective illness, need to be kept in mind. In relatives of patients with bipolar disorder and schizoaffective disorder, rates of bipolar, schizoaffective, and unipolar disorders were greater in the more recent cohorts (16). Further, in the study sample of the NIMH Collaborative Program on the Psychobiology of Depression, the more recent cohorts of bipolar patients were younger at the onset of illness than the older patient cohorts (17). It has been suggested that in the lithium era, such cohort effects reflect awareness of bipolar diagnosis earlier in a patient's history (18).

Prevalence of Mania in the Elderly

Manic syndromes are relatively common among elderly psychiatric patients. Mania or hypomania is said to constitute 5%–10% of the diagnoses of elderly patients referred for treatment of affective illness (19). Roth (20) studied patients admitted for psychiatric hospitalization after the age of 60 years; 6% in his series had manic episodes. In the series of admissions studied by Yassa et al. (13, 21), 4.9% of the psychiatric patients over the age of 60 years were manic. Prevalence data on the elderly reflect both patients with recurrent early-life illness and patients with late-onset illness.

Kramer et al. (15) did not detect a current manic syndrome in any of 923 ambulatory community residents aged at least 65 years for whom interview data were obtained as part of the ECA study. This finding was subject to methodologic limitations of cooperation and exclusion of symptomatic syndromes (22) and might also have reflected movement of manic patients out of the community.

Milder forms of mania, including hypomanic and cyclothymic states, may be managed in an outpatient setting. These cases will therefore be underrepresented among hospitalized patients, such as the sample of Spicer et al. (23). There are few available data concerning type II and other bipolar variants among the elderly in the community. Reich and associates (personal communication, 1989) have noted a lower prevalence of type II bipolar disorder in relatives over the age of 40 than in younger relatives of probands with affective disorder.

Incidence of Mania in the Elderly

Theoretical interest focuses on whether there is a change in the true incidence of mania with aging. Pending availability of the results of studies we have mentioned, it remains uncertain whether the risk of developing mania increases, decreases, or remains the same with increased age. Wertham (24) reviewed 2,000 cases with regard to age at first hospital admission for mania; he noted a decline in admissions of manic patients over the age of 50. On the basis of these data and her own (25), Clayton (26) concluded that the risk of mania declines, or at least does not increase, with aging. This is consistent with the findings of a retrospective study of hospital inpatients by Loranger and

Levine (27); however, these investigators excluded an unspecified number of elderly patients with medical illnesses that were judged to be possibly contributory to the affective episodes.

In contrast, Spicer et al. (23) reported that when all admissions to National Health Service psychiatric hospitals in England and Wales during a 2-year period were considered, there was an increase in first admissions of manic male patients, but not female patients, who were over 60 years of age. The fact that explicit diagnostic criteria were not cited suggests that some demented or delirious patients or those with organic mood disorders may have been included; also, patients lacking prior depressive episodes might have been excluded. The authors' findings are consistent, however, with a more recent report by Eagles and Whalley (28), which indicated a gradual increase with age in first admissions of manic patients of both sexes to Scottish hospitals—more so for men. This increase was sustained for patients past the age of 70. In both sexes the association with age was weaker for mania than for depression.

A remarkably late age at onset of the first manic episode has been reported in elderly manic patients. It was found to be the fifth and sixth decades in the retrospective studies of Shulman and Post (12), Glasser and Rabins (29), Young and Jain (11), and Stone (14) and the prospective studies of Broadhead and Jacoby (30) and Young et al. (31).

The studies we have cited involved treated populations. There are no data concerning incidence in the general community.

ETIOLOGY AND PATHOPHYSIOLOGY

Etiologic Factors in Late-Onset Illness

Bipolar disorder is at least as strongly associated with hereditary factors as is major depression (32). As in major depression (33), most investigators have found that probands with late-onset bipolar disorder have a lower rate of affective disorder among their relatives than do probands with early onset; this was true in samples of patients of mixed ages (17, 34–36) and of geriatric patients (12, 14, 29). Further, age at onset of illness may breed true (unpublished paper of J.R. DePaulo et al.).

Yassa et al. (21) noted a high rate of recent disruptive life events among 10 geriatric manic inpatients. All of these patients had late-onset illness; no comparison with an early-onset group was attempted, however.

Medical and neurological disorders, drugs used to treat these disorders, and drugs of abuse are associated with cases of mania in which the age at onset is greater than 40 years. In such patients, Krauthammer and Klerman (9) noted a relatively low familial rate of affective disorder. Such cases represent a potentially valuable model for understanding idiopathic cases (8, 37). Comparison with idiopathic cases to test the nosologic validity of organic mood disorder, manic, remains limited to a few retrospective investigations (10,

38, 39) and the follow-forward study of Shulman et al. (40). In this last study, geriatric "secondary" manic patients were at increased risk for both rehospitalization and institutionalization.

Manic inpatients aged 60 years and older with onset of the first manic episode after age 58 had antidepressant pharmacotherapy associated with their index episode more often than did elderly manic patients with onset at an earlier age (41). This retrospective finding suggests that in geriatric patients, later age at onset may be associated with different response to antidepressant drugs. Interestingly, it contrasts with an observation regarding patients of mixed ages by Nasrallah et al. (42) that younger age and earlier age at onset were associated with mania occurring during antidepressant treatment.

Kay et al. (43) and Post (19) have proposed that major depressive episodes with onset in late life reflect distinct pathophysiologies and etiologies and that, in particular, degenerative changes in the brain might play an important etiologic role in such cases. Shulman and Post (12) reported that the onset of manic states in the geriatric age range was associated with clinical evidence of coarse brain diseases, particularly in men. This sex difference was not found by Shulman et al. (40), however. Stone (14) noted evidence of "organic cerebral impairment" among 22 of 92 elderly manic inpatients studied retrospectively; 14 of these demonstrated memory dysfunction.

Normal aging is associated with morphologic brain changes. Computerized tomography, for example, shows that ventricle-brain ratio and cortical sulcal width increase with age (44). Differences in brain morphology between bipolar patients and control subjects have been reported both in younger adults (45, 46) and in the elderly (30, 47). Abnormalities have also been noted with magnetic resonance imaging (MRI) of the brain in elderly patients with mania (48).

Although in patients with late-life depression those with late onset have greater brain imaging abnormalities (49, 50), a relationship between age at onset and brain morphologic abnormalities in mania has not been established (30, 47). The cases studied by McDonald et al. (48) had a late age at onset.

Manic symptoms can occur in the setting of cerebrovascular disease, as well as other focal brain lesions (51). Right-side lesions have been particularly implicated in the pathogenesis of mania (52).

Pathophysiology

Abnormalities in central neurotransmitter function, particularly that of catecholamines and acetylcholine, have been implicated in bipolar disorders. The evidence consists of effects of drugs associated with mania and those used to treat it, as well as laboratory measures reflecting these systems (53, pp. 417-502; 54, 55).

Age. These same neurotransmitter systems are vulnerable to age-associated processes (56). Differences in catecholaminergic metabolite measurements between

older patients with major depression and control subjects are reportedly greater than between younger patients and control subjects (57). Neurotransmitter-related measures in older bipolar or manic patients have not been reported.

Late age at onset. Differences in peripheral neurotransmitter-related enzyme activity (58) and neuroendocrine function (59) between geriatric patients with late-onset major depression and those with early onset have been reported. Differences in such measures between bipolar patients with different ages at onset have apparently not been reported.

PSYCHOPATHOLOGY

Manic Affective Features

The manic syndrome is phenomenologically "positive." That is, the predominant affective signs and symptoms represent acceleration and/or excesses of behavior, mental activity, or emotion. In contrast to depression, these changes may in part run counter to those associated with increased age. Whether clinical detection/identification of manic or hypomanic syndromes in the elderly can be more sensitive and accurate than that of depression has not been studied.

Age. Modification of manic affective features by age-associated processes has been postulated. Post (19) suggested that elderly manic patients less often have typical flight of ideas than do younger patients. Slater and Roth (60) commented that many cases of mania in old age are "relatively mild." According to their experience, euphoria in older manic patients is often not "infectious," and speech and thought lack the typical "sparkle and versatility" and are commonly "threadbare and repetitious"; on the other hand, "hostility and resentment" are often marked.

These descriptions of elderly manic patients were clinical impressions presented tentatively (61) and were not derived from empirical investigation. Further, the distinction between late-onset and early-onset cases was not made.

Among 40 symptomatic inpatients of mixed ages studied prospectively (62), only four of whom were in their seventh decade, examination of Mania Rating Scale scores gave limited support to earlier impressions. A statistically significant negative association between age and scores on the activity-energy item of the Mania Rating Scale was noted. This finding was consistent with the suggestion by Gurland (63) of relative psychomotor slowness in aged patients with various psychiatric syndromes, not only depression. There was a low negative correlation between age and scores on the language-thought disorder item and a nonsignificant negative correlation between age and scores on the sexual interest item.

Similarly, for a group of manic patients aged 60 years and over who were studied prospectively (30), total scores on the Blackburn Scale for manic psychopathology at ad-

mission to the hospital were lower than those for young adult patients. Older patients had lower scores on the religiosity item of the scale; however, other items did not differentiate older and young patients.

In our own prospective work, relationships between age and aspects of psychopathology were noted in preliminary findings (31). Older patients tended to have lower Global Assessment Scale (GAS) scores when symptomatic. For symptomatic manic patients, there were significant positive associations between age and higher scores on the elated mood and impaired insight items of the Mania Rating Scale and negative correlations between age and scores on the initiating and making plans items of the Blackburn Scale. At discharge, there were negative associations between age and scores on the (increased) sexual interest and (abnormal) appearance items of the Mania Rating Scale and on the careless dress and grooming and impulsive items of the Blackburn Scale.

Late age at onset. Information concerning differences in affective features in groups of patients with differing ages at onset of illness is similarly scant. In a retrospective study (11), geriatric manic patients with later onset had lower overall dysfunction rated with the GAS. Another retrospective report (29) noted no such differences in psychopathology between same-age patients with late onset and early onset. Broadhead and Jacoby (30) noted higher average ratings on the happiness and cheerfulness item of the Blackburn Scale for late-onset than for early-onset cases. Preliminary prospective data from our center suggest less residual psychopathology at discharge, as measured by the Blackburn Scale, and greater change in Mania Rating Scale scores among late-onset patients than among elderly early-onset patients, and higher ratings on impaired insight on the Mania Rating Scale at hospital discharge among late-onset patients (31).

Dysphoria and Mixed States

Dysphoric mood and other depressive signs and symptoms are not uncommon in mania. These have received limited investigation in the geriatric population.

Age. Post (19) suggested that older manic patients exhibit concomitant depressive features more often than do younger patients. This suggestion was based on clinical experience.

In the study by Broadhead and Jacoby (30), there were equivalent mixed features in the elderly and the young manic patients. On the other hand, in that study a greater proportion of the elderly manic patients than of the young manic patients suffered a depressive episode after resolution of mania but before hospital discharge; this difference was statistically significant.

Late age at onset. In one preliminary retrospective study (11), later-onset elderly manic patients had more dysphoric mood than did earlier-onset elderly patients. However, Broadhead and Jacoby (30) found no difference in depressive features during the manic episode between late-onset and early-onset elderly manic patients.

Delusions and Other Psychotic Features

Mania is often accompanied by delusional ideation (64). Hallucinations can also occur.

Age. Post (19) stated that compared to younger patients, geriatric manic patients more often have persecutory delusions that are not mood-congruent. This assertion, based on clinical observation, has received little investigation.

A prospective assessment of manic inpatients of mixed ages did not reveal an association between age and the presence or absence of hallucinations and/or delusions (64). Further, evaluation of geriatric manic patients did not reveal differences in psychosis when they were compared to younger adults in the study by Broadhead and Jacoby (30). Preliminary evaluation of our prospectively studied sample revealed a significant negative association between age and ratings on the grandiose delusion item of the Blackburn Scale (31).

Late age at onset. Rosen et al. (65) reported a negative association between psychotic symptoms and late age at onset among bipolar patients of mixed ages. Angst et al. (66) reported that in bipolar patients of mixed ages, those with mood-congruent psychotic features were older at onset than those with mood-incongruent features.

In geriatric patients, a positive association between delusions and late age at onset has been suggested for major depression (67). No such association has been suggested for geriatric manic states (30, 31).

Cognitive Dysfunction

Affective illness states can be associated with both subjective and objective evidence of decreased cognitive performance. This impairment in performance can resolve with remission of the affective state. Although the literature regarding such pseudodementia has focused on depressive syndromes, an important association between reversible cognitive dysfunction and mania has also been cited (5, 19, 60). Disorientation and even delirium (60) have been described in manic patients.

Clinicians have disagreed on the relation between age and cognitive dysfunction in mania. Some have indicated that such dysfunction is particularly important in older patients (19, 60).

Neuropsychological investigations of bipolar patients of mixed ages have found deficits in attention and memory during manic states (68, 69). Cognitive dysfunction has also been reported in treated, remitted bipolar patients of mixed ages (46, 70). Cognitive dysfunction in bipolar patients has been related to history of neurological disorder (71) and to brain morphology on MRI (46).

Age. Savard et al. (70) reported that cognitive performance of bipolar patients in remission who were older than 40 years was significantly poorer than that of control subjects of the same age. Broadhead and Jacoby (30) commented that a greater proportion of elderly than of young manic patients performed in the demented range on the Kendrick neuropsychological

battery. However, they noted a large discrepancy between verbal and performance IQ in both groups. In preliminary findings from our prospective study (31), elderly patients tended to score lower than younger patients on the Mini-Mental State examination at hospital admission and had significantly more impaired Haycox Scale assessments of behavioral competence at both admission and discharge.

Late age at onset. In a preliminary retrospective study of geriatric manic inpatients (11), those who were older than 58 years at the time of the first manic episode more often showed evidence of cognitive dysfunction in routine clinical evaluations when they were acutely symptomatic than did patients with earlier onset. Neuropsychological testing had not been performed, however.

Stone (14) reported that evidence of "cerebral organic impairment" was present in 24% of elderly manic patients and that more than 60% of these patients had memory impairment associated with the manic episode. Cerebral organic impairment was associated with late age at onset.

Broadhead and Jacoby (30) noted no significant difference in neuropsychological test battery results between early- and late-onset elderly manic patients. A tendency for patients with late onset to show more evidence of cerebral organic impairment was not statistically significant.

The strategy of testing cognitive function both during episodes of illness and on follow-up, when patients are in affective remission, is important to future work with elderly patients. It permits retrospective assessment regarding state-dependent versus persistent cognitive dysfunction. Since a greater proportion of elderly depressed patients with "reversible" cognitive dysfunction than those without may develop persistent cognitive dysfunction/dementia on follow-up (72), this issue needs to be examined in manic syndromes of late life.

AFFECTIVE COURSE

Greater age may be associated with differences in the course of illness in geriatric patients. Late onset compared to early onset of illness may also be associated with differences in the course of illness in these patients.

Resolution of the Acute Episode

Early studies by Roth (20) suggested a poorer outcome for elderly patients with bipolar illness than for those with other "functional" disorders. He reported on 28 geriatric inpatients with mania in the pre-lithium era who were studied retrospectively. Of those still living at 2-year follow-up, 65% had remained in the hospital. This was a poorer outcome than that of geriatric depressed patients. As in the case of the depressed patients, however, the manic patients were more often discharged from the hospital during this interval than were demented patients. Dhingra and Rabins (73) commented that the outcome of geriatric mania has im-

proved since the investigations by Roth were carried out; presumably this reflects, in part, modern pharmacotherapy. Stone (14) noted episodes lasting 2–13 years in five of 92 geriatric manic patients.

Age. There is little information on whether the rates of recovery from mania are different for elderly and younger patients. Post (19) stated, on the basis of clinical impressions, that elderly manic patients are particularly slow to regain insight.

Several investigators (24, 74, 75) have noted a positive association between age and duration of the acute manic episode in populations of mixed ages, even though only a limited portion of these patients were elderly. Wertham's 2,000 patients (24) ranged in age up to the eighth decade. In MacDonald's sample (74), 12 of 451 patients were 60 years of age or older, and in Lundquist's sample (75), 11 of 103 manic patients were older than 50 years.

Chronic mania has been associated with increased age (24, 76). Wertham (24) noted that seven patients with manic episodes lasting at least 5 years ranged in age from 31 to 60 years. Henderson and Gillespie (76) noted an association between chronic mania and an age of more than 40 years. Indeed, among Lundquist's patients (75), fewer of those aged more than 40 years (84%) than of younger patients (95%) recovered.

Himmelhoch et al. (77) did not find an effect of age on recovery from mania in 81 patients studied retrospectively, although all were aged 55 years or more. In the prospective study by Broadhead and Jacoby (30), there was no difference in duration of the index manic episode between older patients and a group of younger patients. The reports of Stone (14) and Dhingra and Rabins (73) did not examine age effects.

Late age at onset. In the literature on patients of mixed ages, some reports suggest an association between greater age at onset and greater duration of episode and/or chronicity. However, the design of the studies does not permit differentiation of associations with age at onset from those with age alone. MacDonald's patients (74), as well as Lundquist's (75), were selected on the basis of first psychiatric hospitalization. In Wertham's study (24), four of seven chronic patients were aged 38–60 years at the onset of their illness.

In the geriatric literature, neither the report of Broadhead and Jacoby (30) nor that of Stone (14) indicated differences in duration of episode between late-onset and early-onset geriatric manic patients. In our own preliminary studies (31), as we have noted, patients with late-onset episodes had somewhat less residual symptomatology at discharge than did early-onset elderly patients. Dhingra and Rabins (73) and Shulman et al. (40) did not comment on duration of the index episode in relation to age at onset.

Relapse

Differing factors may be associated with chronicity and relapse in geriatric affective disorders (78). While some data are available on geriatric depression, there

is need for data concerning relapse of mania and bipolar disorder in the elderly. Roth (20) did not assess relapse. Young and Jain (11) noted that over 2–3 years, 23 (58%) of 40 geriatric bipolar patients required rehospitalization.

Age. An association between greater age and shorter intervals between episodes was noted by MacDonald (74) in bipolar patients of mixed ages.

Late age at onset. For patients of various ages with bipolar disorder, an association of shorter intervals between episodes with greater age at onset was noted by Angst et al. (66). Also for patients of mixed ages, Swift (79) reported an association between age greater than 40 at onset of illness and shorter intervals between episodes. The patients studied by MacDonald (74) were first admissions, so greater age at onset cannot be dissociated from greater age as a correlate of shorter intervals between episodes in that report.

Among geriatric patients, Stone (14) reported increased frequency of readmission, over 1-month to 10-year follow-up, for those with histories of previous affective episodes than for those without such a history. On the other hand, Shulman et al. (40) found that an age at onset greater than 55 years predicted decreased time to psychiatric rehospitalization at 3- to 10-year follow-forward. Dhingra and Rabins (73) reported no difference in relapse rate over 5–7 years between early- and late-onset geriatric manic patients.

NONAFFECTIVE OUTCOMES

Specific nonaffective outcomes in geriatric bipolar disorders also need study. Clinical predictors of specific outcomes may differ depending on age at onset of illness as well as on age itself.

Mortality

Severe manic states can be life threatening. Decreased sleep, impaired nutritional status through overactivity and distraction, and decreased compliance with medical regimens all pose a threat to the health of the frail elderly patient. Although deaths from “manic exhaustion” were reported to occur most often among young patients (80), reports such as this have not defined the age distribution of the total patient sample examined. Hypomanic states presumably carry less risk. The incidence of manic exhaustion has apparently been reduced dramatically in the psychopharmacologic era (81).

Suicide is a mechanism for increased mortality that is associated with bipolar disorder and with increased age. This has not been studied prospectively in geriatric patients with bipolar disorder.

The observed mortality rate for elderly bipolar patients appears to be greater than the base rate for this age group in the community (73). In Roth's early study (20), the mortality rate over 2 years following psychiatric hospitalization was 11%; this was lower than that for elderly demented patients but was higher than that for depressed

patients of the same age. There were two deaths among nine patients followed by Yassa et al. for 2 years (21). In the study by Stone (14), the mortality rate over 2 years was 16% for geriatric mania. In the study by Dhingra and Rabins (73), mortality at 5- to 7-year follow-up was 34%; these authors commented that the survival rate was significantly lower than the expected rate calculated from census data. Similarly, Shulman et al. (40) found that the mortality rate of geriatric manic patients exceeded that of geriatric depressed patients.

Age. Mortality among elderly patients has apparently not been compared to that among younger bipolar patients in the same study. There is evidence for greater mortality among bipolar patients of mixed ages—at least among those with medical illness (53, p. 151)—than among the general population.

Late age at onset. Neither the study by Dhingra and Rabins (73) nor that of Shulman et al. (40) detected differences in mortality between geriatric patients with late onset of illness and patients of the same age with early-onset illness. Stone (14) did not comment on this issue.

Cognitive Dysfunction/Dementia

A proportion of elderly manic patients develop cognitive impairment and/or dementia on follow-up. Stone (14) reported that 3% of 92 geriatric patients with mania went on to develop moderate to severe dementia over an average of 3 years of follow-up. Dhingra and Rabins (73) noted that at 5- to 7-year follow-up, 32% of elderly manic patients had Mini-Mental State examination scores in the cognitively impaired range (less than 24), and 20% had been placed in nursing homes. These authors commented that this was greater than the 1%–2% per year incidence of all forms of dementia expected in this age group in the community (82). The rate for geriatric manic patients was not greater than that for geriatric depressed patients, however.

Age. Emergent dementia occurs relatively infrequently in bipolar patients of mixed ages, but it has received limited study as an outcome (46), and then in combined unipolar/bipolar samples. In the study by Astrup et al. (83), less than 5% of patients with affective disorders were clinically demented on 7- to 19-year follow-up. This is lower than the rate for geriatric patients suggested by the data of Dhingra and Rabins (73).

Late age at onset. It is not known whether late-onset manic patients are at greater risk for development of cognitive dysfunction/dementia than early-onset elderly patients. Dhingra and Rabins (73) could not detect differences in cognitive impairment, as assessed by Mini-Mental State scores, between patients with late-onset mania and geriatric patients with early-onset mania at 5- to 7-year follow-up.

TREATMENT

A general discussion of management of mania in the elderly is beyond the scope of this article. The somatic

treatment modalities used are not unique. Lithium salts are the drug of choice.

The optimal use of lithium salts and alternative somatic treatments has not been delineated in this age group. In the elderly, consideration must be given to factors that influence both drug pharmacokinetics and pharmacodynamics (84).

Pharmacokinetics

Lithium is hydrophilic. It is renally eliminated.

Age. Reduced lithium clearance can be associated with increased age (85). The volume of distribution, because of increased fat/lean body mass ratio, may also be reduced. Further, greater age is associated with additional factors, such as diseases and drug treatments, that can affect lithium excretion (84, 85). These changes necessitate use of lower doses of lithium to achieve equivalent plasma levels.

Late age at onset. This factor has not been examined as a correlate of lithium pharmacokinetics. Onset of mania at a late age may be associated with especially high frequency of physical illness and drug treatments. Therefore, pharmacokinetic changes might be especially frequent in such elderly patients.

Toxicity and Acute Pharmacotherapy

The systematic literature concerning acute treatment of geriatric mania consists primarily of retrospective discussions (14, 29, 77). Some have included demented patients (77).

Reports concerning clinical effects of lithium in geriatric patients have focused mainly on lithium toxicity. Some authors (86, 87) have noted that acute toxic symptoms, including delirium, can occur at plasma levels below 1.5 meq/liter in elderly patients.

Age. While there has been speculation that aging of the brain and other organs renders them more sensitive to lithium, there has been inadequate investigation of this issue. Reports that have included old and young patients have generally not involved comparable lithium levels in the two groups. One important exception is the study by Murray et al. (88), in which more tremor was noted at comparable lithium levels in elderly patients. Since the authors did not assess the patients when they were drug free, they were not able to exclude nondrug causes of tremor. A report of a retrospective study by Smith and Helms (89) noted more moderate to severe side effects, but not total side effects, in elderly patients than in younger patients at comparable lithium levels; neurotoxicity in particular was noted in the elderly patients.

Late age at onset. Late onset may be associated with factors such as medical and neurological disorders and drug treatments that, in turn, predispose to lithium toxicity on a pharmacodynamic basis. These issues, as well as the relationship of late-onset illness per se to toxicity remain open to study.

Efficacy of Acute Pharmacotherapy

Many elderly patients with mania are said to respond well to lithium (13, 14, 29). Clinical experience and the small open study by Schaffer and Garvey (90) suggest that lithium levels below 1.0 meq/liter can be effective in some elderly patients. It is not known, however, whether this is true more often in elderly than in young patients. There also has been no systematic evaluation of the relation of lithium concentrations to therapeutic effects in the elderly population.

Age. Studies of populations of mixed ages have generally not evaluated the effects of age or included many elderly patients. A prospective study (62) indicated trends for positive association between age and scores on the residual language-thought disorder and impaired insight items of the Mania Rating Scale at the third week of hospitalization among older patients from a mixed-age sample who were receiving routine pharmacotherapy, including lithium salts. There was a significant negative association between age and change in scores on the activity-energy and language-thought disorder items between the first and third weeks of treatment. Older patients also were hospitalized longer. In the study by Broadhead and Jacoby (30), fewer elderly patients than younger patients were discharged on a regimen of neuroleptics in addition to lithium. Duration of hospitalization was comparable in the two age groups. In our own preliminary prospective studies (31), elderly patients also did not differ from younger patients in duration of hospitalization.

Clinical predictors of acute response to lithium in younger patients (91) have not been studied in the elderly. One retrospective report (77) suggested that elderly manic patients with dementia respond relatively poorly. However, in the experience of Broadhead and Jacoby (30), concurrent dementia did not adversely affect outcome. Shukla et al. (92) reported poor response to lithium treatment in patients of various ages with organic manic disorders. Black et al. (10) also noted poorer response to acute treatment among patients of mixed ages with mania complicated by serious medical conditions or by other primary psychiatric diagnoses.

Late age at onset. Comparison of response to treatment in late-onset and early-onset elderly manic patients has received minimal investigation. Broadhead and Jacoby (30) did not note differences in therapeutic response in relation to age at onset.

In our preliminary prospective data (31), patients did not differ in duration of hospitalization on the basis of age at onset. However, patients with later onset tended to have lower scores on the Mania Rating Scale and the Blackburn Scale at discharge and greater change from admission Mania Rating Scale scores.

Toxicity and Continuation and Maintenance Treatment

Long-term lithium toxicity, including thyroid dysfunction and possible impact on renal function, has not

been examined specifically in the elderly as a group. Its relationship to age at onset of illness also needs study.

Efficacy of Continuation and Maintenance Treatment

The efficacy of lithium continuation and maintenance treatment in geriatric bipolar affective disorder has not been specifically examined. Such studies are particularly needed in the elderly, since the course of illness in this age group may be more difficult than in younger patients.

Age. One recent negative report (93) concerning the relation between ongoing affective morbidity and duration or age at initiation of lithium prophylaxis apparently dealt with a combined unipolar and bipolar sample. These subgroups were not analyzed separately.

Late age at onset. This dimension has not been examined in relation to the therapeutic efficacy of maintenance and continuation treatment in geriatric bipolar disorder.

CONCLUSIONS

Mania occurring for the first time in late life, with or without antecedent depressive episodes, may differ from bipolar illness in young adulthood. Late-life illness may be more heterogeneous. It appears less directly genetically determined. It may reflect, in part, vulnerability acquired through brain changes and disorders associated with aging. On the other hand, age-associated brain changes also may modify early-onset illness.

Studies of mania in the elderly hopefully will contribute to better diagnosis, to safer and more effective acute treatment, and to improved preventive measures. They are also likely to facilitate our understanding of early-life bipolar disorders.

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From Nurture to Network: Examining Links Between Perceptions of Parenting Received in Childhood and Social Bonds in Adulthood

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***Objective:** The authors' goal was to consider the extent to which key characteristics of their parents influence children's later socialization in terms of social networks and intimate relationships and thus to examine whether there is evidence of such continuity. **Data Collection:** The authors reviewed the pertinent literature and then examined studies using a measure of key dimensions of the parenting received in childhood (the Parental Bonding Instrument) as well as measures of adult social networks. **Findings:** The literature review revealed evidence of links (more evident in women) between perceptions of having received uncaring parenting and deficiencies in diffuse social bonds, which could reflect a causal process, a general response bias, or methodological limitations. By contrast, studies using the Parental Bonding Instrument and a specific measure of adult intimate bonds failed to find links between perceptions of parenting received in childhood and the quality of current intimate relationships unless there was extreme deprivation of parental care; in that case, the current intimate relationship was more likely to be rated as uncaring. **Conclusions:** These findings refine the view that early socialization experiences shape and dictate interpersonal relationships in adulthood. Any deficiencies in parent-child relationships, except, perhaps, gross parental deprivation, appear capable of modification by a range of experiences (particularly subsequent interpersonal relationships).*

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The view that early socialization experiences in the family shape and dictate the structure and function of adult interpersonal relationships (ranging from the most intimate to more diffuse social supports) underlies psychoanalytic, object relations, self psychology, and attachment theories (1). Several empirical studies have been undertaken in the last decade examining evidence of such continuity. The findings have been varied, and we anticipate that the debate over continuity versus discontinuity will be a major focus in social psychiatry because of the capacity for etiological and treatment issues to be refined by the process. In this paper, we shall review representative studies and demonstrate contrasting views about the existence of developmental determination of adult interpersonal relationships.

Because both early family influences and adult social support systems are intrinsically broad and nebulous

constructs, some restriction of definition is required. In this paper we examine the proposition that exposure to dysfunctional parenting is associated with negative social bonding in adulthood, as hypothesized by a number of authors (2, 3). Even this limited proposition, however, assumes the relevance of early family influences to all subsequent adult interpersonal relationships, without qualification as to issues such as the number, breadth, and degree of intimacy of different relationships in later life.

Theoretically, dysfunctional parent-child bonding might emerge from ongoing dysfunctional relationships and/or from prolonged or traumatic parent-child separations (e.g., following parental death or divorce). After several decades of research, it remains quite unclear whether parental separation per se predisposes the child to disruption and conflict in adult intimate relationships (4, 5), largely because of the many intervening modifying variables (especially inadequate parenting before and after the actual separation). Thus, we favor a focus on parental function rather than family structure because dysfunctional parent-child attachment is likely to be a more potent pathogenic variable, not only for individuals who experience parental separation but also for those who do not.

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CONTINUITY THEORISTS

Bowlby, the most prominent of the attachment theorists, proposed a continuity hypothesis broadly suggesting that an individual's experiences with his or her parents strongly influence any later capacity to form affectional bonds. Bowlby (3) suggested that all later interpersonal experiences are evaluated by the individual in terms of their capacity to accentuate or attenuate developmental pathways that result from early child-parent experiences. Until recently, empirical research on attachment has focused almost exclusively on early childhood, but, for Bowlby (6), "attachment behaviour is held to characterize human beings from the cradle to the grave."

By way of mechanisms, Bowlby described "mental models" constructed by the child on the basis of experiences with significant others. These mental models represent composites of expectations and beliefs about the self and the trustworthiness of others: "Whatever expectations are developed during those years tend to persist relatively unchanged throughout the rest of life" (7). Although later attachment experiences may serve to modify such expectations, childhood experiences are viewed as the principal determinants of abnormalities in adult attachments and, consequently, any resultant increase in psychopathology (notably anxiety and depression).

More recent research has taken attachment theory and its predictions beyond early childhood. Main et al. (8) assessed parents' working models of attachment based on retrospective descriptions of their own childhood experiences and the quality of their own child's attachment. Main et al. assigned adults to attachment groups on the basis of the Adult Attachment Interview, in which assessment was dependent on both "ease" and "content" of recall. Parents who were rated as secure in their own childhoods were reported to have secure attachments with their own infants. For Main et al. these effects need not be stable; some parents whose childhood attachments were insecure demonstrated the ability to cognitively work through negative issues, allowing them to become sufficiently secure in their own parenting skills and resulting in an improved capacity to produce secure offspring.

In contrast to the focus of Main et al. on representations of childhood experiences as influences on subjects' own characteristics as parents, Hazan and Shaver (9) focused on subsequent love relationships or adult intimate relationships. They conceptualized romantic love as an attachment process and developed a self-report procedure to differentiate adult attachment styles. Consistent with the authors' hypotheses, adults categorized as insecure (i.e., ambivalent and avoidant) in their most important romantic relationships reported more negative expectations and beliefs about love, histories of shorter romantic relationships, and less favorable descriptions of their childhood relationships with their parents than did adults who were categorized as secure in their most important romantic re-

lationships. Notwithstanding methodological limitations, the studies of Main et al. and Hazan and Shaver support the utility of extending the attachment perspective to the examination of evidence of links between parent-child bonding and subsequent social attachments in adulthood.

KEY DIMENSIONS AND MEASURES OF PARENTING

As suggested, there are immediate and predictable problems in attempting to measure parent-child bonds and attachments, making it difficult to come to firm conclusions about continuity. Assistance emerges from the numerous multivariate studies (10-12) that have refined central constructs underlying parental attitudes and behaviors. The dimension of "care" has been generated consistently as a principal element, and the next most consistently generated dimension is variably termed "overprotection" or "control." Such dimensions appear fundamental and not limited to parental characteristics. Hinde's review (13) indicated that the dimensions of care and control underlie all important interpersonal relationships, be they parent-child, marital, teacher-pupil, or therapist-patient.

In terms of measures of such parental characteristics, Gerlsma et al. (14) recently reviewed 14 factor-analytically derived measures of parental style and concluded that only three met basic psychometric criteria—the Children's Reports of Parental Behaviour Inventory (15), which is completed by children, the Parental Bonding Instrument (11), and an inventory for assessing memories of parental rearing behavior (16). The latter two are completed retrospectively by adults, and all three measure the constructs of parental care and overprotection.

We reviewed studies using the Parental Bonding Instrument because it is the only one of the three measures used in continuity research and because its reliability and validity have been examined extensively and encouragingly. The Parental Bonding Instrument is a 25-item self-report questionnaire asking subjects to rate their parents as they remembered them in their first 16 years. Ratings for maternal and paternal care and overprotection are generated on a 4-point Likert-style scale; parents may be assigned to one of four contrasting styles, the most pathogenic of which is "affectionless control" (low care, high overprotection) (17). The Parental Bonding Instrument is highly reliable and insensitive to the effects of the respondent's mood, and there is considerable support for its validity as a measure of both actual and perceived parenting in studies using family corroborative witnesses, in twin studies, and in those using independent raters (18).

It is likely that anomalies in parental care and overprotection influence the development of children by somewhat differing mechanisms. The dimension of parental care has been central in the formulation of theories of early socialization and is given expression in the concept of attachment. Bowlby (19) felt that secure in-

fant attachment was most likely to follow the infant's experiencing the caregiver as a reliable source of comfort and as responsive, available, and sensitive. Indifference or rejection on the part of the attachment figure is held to be associated with anxious/ambivalent attachment by the infant. Additionally, deficient care is the parental characteristic most frequently imputed as disposing the child to later psychiatric disorder, and consequent low self-esteem is viewed as a central mediating variable (17). Overprotection (as measured by the Parental Bonding Instrument) is not synonymous with excessive care but is a construct reflecting control, intrusion, infantilization, and encouragement of dependency and is held to have its main deleterious effects by slowing or restricting the child's necessary socialization (17).

Studies Linking Parental Bonding Instrument Ratings With Measures of Adult Social Networks

As noted, studies that have attempted to determine links between Parental Bonding Instrument ratings and measures of the adult social network assume connections between very intimate relationships in childhood (parent-child) and a series of adult relationships that vary widely in terms of their significance and perceived intimacy. Their varying saliency may well influence evidence of links, as we will detail.

Our view of social support parallels that advanced by Sarason et al. (20), who went beyond a concept of social support as an "environmental provision," arguing that it may be viewed more appropriately as an individual difference variable, reflecting a perception of being accepted, loved, and valued (20).

Sarason et al. (20) had 251 college students complete the Parental Bonding Instrument as well as the Social Support Questionnaire, a measure of the number of and satisfaction with available support figures. They confirmed hypotheses formulated in accordance with Bowlby's theory of developmental continuity (21): Parental Bonding Instrument care ratings were positively related to Social Support Questionnaire ratings and Parental Bonding Instrument overprotection ratings were inversely related to Social Support Questionnaire ratings. Given the retrospective nature of the study, the students' reports of childhood may have been distorted by their current level of satisfaction, so the researchers applied a "correction factor for optimism." With this adjustment, they found that correlations between Social Support Questionnaire and Parental Bonding Instrument ratings declined minimally and concluded that, although they were unable to rule out the possibility of a recall bias, their findings suggested that a general tendency to evaluate one's own life in negative terms was unlikely. They also concluded that their findings suggested the importance of the quality of parental involvement with children in terms of a child's later sense of "social embeddedness."

Sarason et al. (22) reported three additional studies. In the first, Parental Bonding Instruments completed by 217 undergraduate psychology students were intercor-

related with a number of self-report measures of social support. Parental Bonding Instrument ratings (particularly those for parental care) correlated positively and strongly with ratings on the Social Support Questionnaire, weakly with ratings on the Inventory of Socially Supportive Behaviors (measuring the frequency of receiving supportive behaviors in the past month), and strongly with ratings on the Family Environment Scale (a measure of currently available social support from the family). The strong correlations between Parental Bonding Instrument ratings and ratings on two of the measures in a group of students might suggest that findings were confounded by the fact that the students' parents represented a major part of the students' social networks, thus contributing to or determining the positive associations. Arguing against this interpretation, Sarason et al. reported links between Parental Bonding Instrument care ratings and ratings of the "percentage of confidants" on the Social Network List when parents were excluded as confidants, indicating that subjects who were recipients of higher parental care also had a higher percentage of confidants in their social network.

In their second study with the same group of students, Sarason et al. (22) reported that high ratings on the Social Support Questionnaire, the Interpersonal Support Evaluation List, and the Perceived Social Support (from friends and family) measure were associated strongly with both high parental care and low parental overprotection ratings on the Parental Bonding Instrument for female respondents but with only high parental care ratings for male respondents.

In their third study with the same sample, Sarason et al. (22) interviewed the students about social support issues, using measures such as the Interview Schedule for Social Interactions (23) to assess the availability and adequacy of close, meaningful relationships as well as the extent and adequacy of more extended social support figures. High parental care ratings and low parental overprotection ratings on the Parental Bonding Instrument were consistently linked with ratings of the availability of extended social support figures, but only high parental care ratings on the Parental Bonding Instrument were linked with ratings of the availability of close relationships. Links were not clearly established between Parental Bonding Instrument ratings and perceived adequacy of social support according to either measure.

These several studies undertaken in essentially normal adults suggest links between the type of parenting received in childhood (especially parental care) and several measures of social support. Three broad explanations of those links, central to this review, could be 1) incorporation of parents into both the Parental Bonding Instrument and the social support measures, creating spurious links, 2) a general response bias toward rating all interpersonal relationships positively or negatively, or 3) a true link between the quality of parenting received and current social support levels. Several similar study designs will now be considered in terms of each explanation.

Flaherty and Richman (1) had 211 first-year medical students complete the Parental Bonding Instrument and the 11-item Social Support Network Inventory, which rates availability, instrumental support, emotional support, event-related support, and reciprocity of the "five most important members" in the respondent's social network. Respondents with higher social support ratings gave both parents significantly higher care ratings and their mothers lower overprotection ratings. Recognizing that the original analysis included family members and the "possible overlap of the effects of parents in both the independent and dependent variables," Flaherty and Richman repeated the analyses after excluding all relatives from the social support measure. Higher social support ratings were still associated with significantly higher parental care ratings; the significance of the ratings for maternal care was stronger than that of the ratings for paternal care. The authors concluded that "the capacity to develop adult supportive relationships is affected by the earlier experience of parental warmth." The operation of a response bias was rejected on the basis of failure to find a link between Parental Bonding Instrument overprotection ratings and social support levels.

Parker and Barnett (24) had a sample of 129 women complete the Parental Bonding Instrument and the Interview Schedule for Social Interactions within 3 weeks of hospital discharge after giving birth to their first child. These women again completed the Interview Schedule for Social Interactions 12 months later. The subjects' ratings on the Parental Bonding Instrument of the care they received from their mothers were significantly linked with their ratings of the availability of close, meaningful relationships and the availability of extended social support figures on the Interview Schedule for Social Interactions on both occasions of testing. However, after the subjects' "neuroticism" ratings (suspected as reflecting a plaintive-set response bias) were partialled out, there was a significant link only between their ratings of the maternal care they received and their ratings of the current availability of close relationships.

Flaherty and Richman (1) suggested that their data were "congruent with the psychodynamic assumption that late affective modes of relating are linked to the quality of earlier object relations." The findings of both their study and ours, however, could be explained by some subjects incorporating their mothers in the Interview Schedule for Social Interactions measure. A general response bias is a less likely explanation because links were restricted to maternal characteristics and not evident in the paternal analyses.

Studies Examining Links Between Parental Bonding Instrument Ratings and Measures of Intimate Relationships

Truant et al. (25) examined links between early parent-child relationships and quality of marriage among 124 subjects who consecutively attended a Canadian family medical center. These subjects rated their par-

ents (and other parental figures) on the Parental Bonding Instrument and their spouses on the Locke-Wallace measure of marital quality. Importantly, these subjects' ratings of maternal and paternal care and overprotection on the Parental Bonding Instrument were not significantly linked with their ratings of marital quality. However, consistent and significant correlations were found for selected subgroups. Poor marital quality was linked with low care ratings on the Parental Bonding Instrument in the case of the "least caring parent" (50% fathers, 40% mothers, 10% others) most clearly for female respondents and after the effects of neurotic symptoms were controlled. (Neurotic symptoms were controlled to exclude the influence of a general negative response bias.) For the whole sample, the strongest correlations emerged in the presence of major childhood separation experiences, but correlations were also observed among a subgroup of female subjects who did not have such "risk" factors to marital quality as major separations in childhood, previous marriage, or current or past emotional illness. Truant et al. suggested that the failure to find links between marital quality and perceived mothering and fathering and the finding of such links for the "least caring parent" or parent figure may reflect the greater influence of a negatively perceived relationship than of "the protective influence of a coexisting good relationship." Thus, they held that their results were consistent with an "interactional model," where early childhood experiences can exert an effect on later adult marital quality but are most likely to do so when childhood adversity (e.g., childhood separations) has occurred.

Truant et al. reported that evidence of developmental continuity appeared limited to psychologically well women; it was not readily apparent in men or psychologically unwell women. Although such selectivity is consistent with the study of Sarason et al. (22), it is contrary to the basic tenets of attachment theory. It has been argued that mate selection among men may be more influenced by physical appearance (26); therefore, men may be less influenced by childhood experiences when forming attachment relationships in later life.

The Intimate Bond Measure (27) was developed in a similar way to the Parental Bonding Instrument as a self-report measure of the care and control exerted by the intimate partner, building on Hinde's recognition of the fundamental importance of such care and control to all interpersonal relationships (13). The developmental study of the Intimate Bond Measure (27) and subsequent research (28, 29) have suggested that this instrument has acceptable validity as a measure of actual and perceived characteristics of the intimate partner and that the care scale (but not necessarily the control scale) is insensitive to depressed mood state.

A series of studies have examined links between Parental Bonding Instrument and Intimate Bond Measure ratings, pursuing one of the fundamental aspects of the continuity hypothesis, namely, that levels of perceived parental care and control relate to similar levels of perceived care and control in adult intimate relationships.

Two contrasting explanations of any links have been pursued: 1) that parental characteristics establish a pattern for adult interpersonal relationships and 2) that any links may be spurious because self-report measures are theoretically susceptible to a number of biases whereby subjects may rate relationships under the general influence of positive (e.g., social desirability) and negative (e.g., plaintive set, assign blame) biases. If either positive or negative biases operate, they will create or inflate correlations between Parental Bonding Instrument and Intimate Bond Measure ratings, unless such biases cancel each other out or are specific to only one relationship (the parent or the intimate partner). Thus, statistical links between Parental Bonding Instrument and Intimate Bond Measure ratings might merely reflect the subjects' particular way of judging relationships. We now note those studies examining links between Parental Bonding Instrument and Intimate Bond Measure ratings.

Hickie et al. (28) had 136 depressive patients complete both measures. A correlation matrix showed no link between parental care and partner care ratings (all correlations were less than 0.19), but there were inconsistent and, at best, weak links between parental overprotection and partner control ratings (the highest coefficient was 0.37, in patients with melancholic rather than nonmelancholic disorders). An analysis of a subgroup of depressive patients who gave "very low" parental care ratings (less than 10 for either parent) revealed a greater chance (odds ratio of 3.1 with a 95% confidence interval of 1.5–6.3) of giving their partners very poor care ratings (less than 10).

In a separate study of patients with nonmelancholic depressive disorders only, Hickie et al. (29) studied 69 patients who had been in an intimate relationship with a cohabiting partner for at least 12 months. When Parental Bonding Instrument and Intimate Bond Measure care ratings were correlated, only one significant association was demonstrated: female patients who gave their mothers high care ratings gave their intimate partners lower care ratings ($r = -0.40$). All other Parental Bonding Instrument/Intimate Bond Measure correlations were less than 0.10. Coefficients for Parental Bonding Instrument overprotection and Intimate Bond Measure control ratings were all less than 0.22. Again, when a separate analysis was made of the patients who gave their parents extremely low care ratings, a weak trend was observed for them to give their intimate partners very low current care ratings (odds ratio=1.8) and very low care ratings for the time before they became depressed (odds ratio=2.4). In both of the studies by Hickie et al., although the perception of a current intimate partner as dysfunctional was associated with a greater risk for nonmelancholic depression, there was no apparent link between that risk and adverse attachment experiences in childhood.

In the two studies of Hickie et al. of patients with clinical depression, most of whom were women, the lack of evidence of developmental continuity is consistent with the findings reported by Truant et al. (25) for

psychologically unwell women. Surprisingly, the attachment hypothesis, which was originally conceived as a possible explanation of suggested links between adverse interpersonal experiences in childhood and psychopathology (particularly depression) in adulthood, seems most difficult to substantiate in psychologically distressed groups, perhaps because vulnerability to clinical depression may be established by a variety of developmental pathways.

Brennan and Wamboldt (30) studied 172 adults attending a private medical center in Washington, D.C. They found that Parental Bonding Instrument care and Intimate Bond Measure care ratings achieved correlations of less than 0.02 and that Parental Bonding Instrument overprotection and Intimate Bond Measure control ratings achieved coefficients of 0.23 and 0.12. The studies of Hickie et al. (28, 29) and of Brennan and Wamboldt (30) confirm findings from an earlier study by Parker and Hadzi-Pavlovic (31), undertaken before the Intimate Bond Measure was developed. In that study, 79 women whose mothers had died when the subjects were children rated their fathers and stepmothers on the Parental Bonding Instrument and their husbands on several items assessing marital affection. The correlations of marital affection ratings with parental care ratings achieved coefficients of less than 0.15. Thus, a series of studies have essentially failed to establish general links between the quality of the parenting received in childhood and the quality of adult relationships.

DISCUSSION

It is currently argued that the experience of secure attachment in childhood increases the likelihood of engaging successfully in adult interpersonal relationships, perhaps because the parent-child attachment promotes a sense of self-worth and a healthy "self-reliance" (19). Conversely, the experience of low levels of parental care and the resulting negative parent-child bonding is held to impair the ability to form close confiding relationships as an adult (19). A poor self-concept and low self-esteem have been suggested as central mechanisms in the latter link, exerting their influence by creating a greater vulnerability to life stressors. Insufficient parental care is held as fundamental in establishing any initial vulnerability, and the impact of overprotective parenting on social competence is considered somewhat less pathogenic, but these dysfunctional parental characteristics are apparently more influential than structural aspects such as parental loss per se. Separation from a parent in childhood has been shown not to constitute a risk if it does not lead to poor parental care (32), and this has been detailed in several reviews (33, 34). The present review builds on such findings, examining particularly the relationship between experiences of different levels of care in early childhood and in adult interpersonal relationships to examine whether the continuity versus discontinuity debate can be clarified and refined.

Support for the general continuity proposition that

parent-child bonding is associated with social bonding in adulthood emerges from studies examining links between ratings of the quality of parenting received and more diffuse measures of the adult social network. It appears most prominent in women and those who are psychologically well. In particular, the quality of parental care received (as measured by the Parental Bonding Instrument) has been shown to correlate positively and strongly with several measures of broad social support (including availability of support figures and number of confidants) and satisfaction levels with such support.

Before acceptance of such qualified support for continuity (i.e., that good parental care in childhood, particularly good maternal care, disposes to a wider and more satisfying social network in adulthood), several noncausal links require closer examination. Reported associations could be a direct result of a failure to distinguish parental from adult social relationships in several studies, general response biases in rating interpersonal relationships, and effects of the subject's personality style or temperament (evoking greater parental care and adult social support). Such confounding issues were overcome in several studies. Although a general "satisfaction" response bias may contribute to the findings in part, residual links favor the hypothesis of continuity between earlier parenting and subsequent social networks, although the mechanism of any such continuity remains speculative.

The Parental Bonding Instrument/Intimate Bond Measure research strategy has allowed us to measure the more specific relationship between the parental care received in childhood and current relationships with an intimate partner without the problem of confounding. Surprisingly, neither continuity links nor evidence of response-set biases (which, if present, would have generated links) have been suggested. Studies using the Parental Bonding Instrument/Intimate Bond Measure research strategy are consistent in their lack of support for the continuity model, except in situations of gross deprivation of parental care, when such respondents were also more likely to rate their intimate partner as extremely deficient in care. Notably, these studies have been conducted in clinical rather than in community samples. Although attachment theory would suggest that continuity is most pertinent to clinical subjects, other factors may influence the findings among patients. A response bias may operate whereby patients may deny associations between past and current relationships. Alternatively, those who are distressed may actually evaluate each relationship more clearly and avoid the "halo" effect often observed in psychologically well individuals. Among clinical patients who report high rates of both dysfunctional parenting and dysfunctional current relationships a ceiling effect may operate so that possible associations between Parental Bonding Instrument and Intimate Bond Measure ratings might have been obscured. The present review clearly suggests the benefit of separating intimate from "other" social support relationships when examining possible differential effects.

Central to the present review has been the concept of bonding. Although it may be argued that the terms "bonding" and "attachment" are similar, there are some important differences. Bowlby (19) argued that the infant is born with a biological propensity to seek attachment to a mother figure and that attachment is an "instinctive" process. Bonding, by contrast, is perhaps best viewed as less clearly biologically determined. The regulation of interpersonal distance is subject to more voluntary and cognitive influences. Rutter (35) suggested that there is a difference between the general tendency to seek attachments and the formation of selective bonds that are personal, social, and reciprocal. Implicit in the distinction is the understanding that processes underlying attachment and selective bonding may be different. Attributes of the adult intimate partner are likely to be essential to the bonding process, so that the final relationship reflects not only the past developmental experiences of the subject but also relevant characteristics of the partner. An overly deterministic view of development fails to concede such current partner effects. As illustrated by the risk factor studies with the Intimate Bond Measure (28, 29), a subject with no developmental vulnerabilities who cohabits with a dysfunctional partner may develop the same psychiatric disorder as a subject who reports both past and current relationships as deficient, so that continuity of negative interpersonal relationships is clearly unnecessary, at least to the onset of depressive disorders.

If the continuity hypothesis for broad social attachment in adulthood is not determined by confounding or by response biases, then some clarification may be emerging. Levels of early parental care influence wider diffuse social networks in adulthood but do not necessarily dictate levels of affection or control in the adult intimate relationship—unless there has been gross early deprivation of parental care.

POTENTIAL EXPLANATIONS OF DISCONTINUITY

Failure to find support for the continuity hypothesis in relation to intimate adult relationships does not require (although it may imply) a rejection of the notion of links between past and present interpersonal relationships. Rather, it suggests the need to acknowledge the potential for modification of developmental patterns. Although experience of low levels of parental care might theoretically create a vulnerability to associate with an uncaring adult partner (when not disposing to actual avoidance of close interpersonal links), several factors may act as modifiers. Brown and Harris (36) emphasized the importance of current circumstances in determining the extent of impact of early experiences. In a complex theoretical model, they identified vulnerability factors that function to increase risk in the presence of a provoking agent. The obvious corollary is that, in general, the lower the rate of provoking agents and vulnerability factors, the less likely it is that support for the continuity hypothesis will emerge. Thus, for

Brown and Harris, the perspective is far from being couched in deterministic terms. The impact of any initial difficulty in the parent-child relationship (e.g., a pervasive negative cognitive bias) can be avoided, or the bias corrected, if the person happens to make a secure attachment at some point. Brown and Harris conceded that to a large extent this is a function of luck. Evidence of discontinuity has been well established with the frequent observation that childhood adversity is not always associated with a poor outcome. For instance, Quinton et al. (37) found evidence for a "cycle of transmitted deprivation." They found that although most of the women they studied who were raised in institutions had higher levels of psychosocial dysfunction and were much more likely to be rated as poor parents in adulthood, some of these women were not poor parents, suggesting the operation of mediating factors—even in conditions of extreme adversity.

The protective effects of a positive marital relationship have been well documented. Good marriages have been described as "health protective," functioning to develop and preserve self-esteem as well as buffering against stress (38). Research has suggested that close affectional ties may be instrumental in modifying the effects of earlier parental deprivation (31, 36). In a longitudinal study of women, Caspi and Elder (39) explored the adult sequelae of difficult behavior in childhood. They found evidence of continuity: difficult behavior in childhood was associated with a greater risk of ill-tempered parenting and poor social control in adult life, but this outcome was contingent on marriage to a nonassertive man. Difficult behavior in childhood made it significantly more likely that women would marry nonassertive men, increasing the likelihood of poor social control. If they did not marry nonassertive partners, no such tendency emerged. These findings suggest continuity extending early life experiences to adult relationships, more specifically to spouse selection. Similarly, Vaillant (40) explored the relationship between earlier childhood experiences, marital relationships, and current psychological health in men and noted that marriage seemed to offer men a chance to overcome previous adverse experiences. That spouse characteristics may function both to maintain or ameliorate maladaptive behaviors has important implications for treatment.

The designs of the studies reviewed here have generally required that subjects be currently or recently involved in an intimate relationship, thereby effectively excluding those whose experience of negative parent-child bonding renders them incapable of engaging in adult intimate relations. There is some evidence, however, that those most in need of the support provided by a good marriage may not be able to benefit from it because the ability to form close relationships may itself be impaired by earlier adversity (41). This failure to establish relationships may prevent us from demonstrating evidence of continuity. As already noted, a negative bonding experience may result in the failure to acquire a true sense of self and resilient self-esteem, attributes

promoting coping in later life. This greater vulnerability may result in the avoidance of close relationships for fear of intimacy, failure, and/or rejection.

Bartholomew (42) has identified two forms of adult avoidance of intimacy. First, a "fearful" style, where a conscious desire for social contact is inhibited by fear of its consequences, and, second, a "dismissing" style, characterized by a defensive denial of the need or desire for greater social contact. Such individuals actively avoid situations of intimacy in an effort to preclude the possibility of rejection. As a result, they undermine the chance of establishing satisfying social relationships, which, empirical evidence suggests, may serve to modify considerably any pattern established by difficulties in early parental bonding (39). For Sroufe (43), later outcomes of earlier experience "may be subtle or complex, taking the form of increased vulnerability to certain kinds of stress, for example, or becoming manifest only when the individual attempts to establish intimate adult relationships or engage in parenting." These sentiments were echoed by Rutter (44), who suggested that certain "adult" events may be necessary to the continuity of adversity from childhood. Rutter et al. (45) suggested that a poor marriage may be an essential factor for the adverse effects of institutional rearing and childhood behavior problems to continue into adulthood.

Undoubtedly, the situation is complex. By restricting the present review to studies using the Parental Bonding Instrument, we acknowledge that conclusions remain subject to the limitations that follow from a reliance on self-report measures. In addition to imperfect memory recall, subjects' reports of childhood relationships may have been biased by subsequent adult history and current life satisfaction. However, as noted earlier, studies investigating the psychometric properties of the Parental Bonding Instrument have found support for its validity as a measure of both perceived and actual parenting over time, thus supporting its construct validity. Further, within the context of the present review, controlling for current life satisfaction (20) and partialling out the effects of neuroticism (25) did not significantly alter associations between Parental Bonding Instrument ratings and outcome measures (adult social support and marital quality, respectively). Thus, given that it is never possible to eliminate the possibility of bias emerging from retrospective recall or other sources, evidence suggests that any such contribution to reported associations is slight at best.

CONCLUSIONS

The concept that early socialization experiences shape and dictate interpersonal relationships in adulthood has, until recently, been viewed as an *a priori* issue rather than one to be investigated empirically. Despite methodological concerns, the present review suggests some refinement to the continuity/discontinuity hypothesis and should assist in the essential task of theoretical and empirical elucidation of the mechanisms and

processes that underlie the varied pathways from childhood to adult life (44). We suggest that some specificity is emerging. First, negative parent-child bonding (in particular, low levels of parental care) may dispose to judging social bonding in adulthood negatively, either directly or through shaping mental models. Second, those exposed to extreme deficits in early parental care appear more likely to associate with an uncaring intimate partner (if a relationship is established at all). Any initial vulnerability established under less extreme difficulties in the parent-child relationship appears capable of being modified by later relational experiences with intimate partners and with significant others. This conceptualization, although at odds with Bowlby's initial view of development (19) (in which outcomes were seen as highly dependent) appears consistent with the dynamic concept of development that is the hallmark of Bowlby's more recent writings (3). Research then needs to focus not only on current relationships but also on relational histories. Although quantitative aspects (number of current and sequential relationships) are important, qualitative aspects are probably more important to study because no optimal number of social support figures can be assumed or presumed. We can envisage a continuum of development where support for the continuity model is strongest in early relational experiences and later positive experiences modify any initial vulnerability and, thereby, facilitate a move toward relational competence. Overall, such findings suggest cause for optimism insofar as there appears to be considerable scope for modification of early patterns, an encouraging conclusion for shaping therapeutic and social policy endeavors.

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AIDS/HIV Risk Behavior Among the Chronic Mentally Ill

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***Objective:** There is growing concern that chronic mentally ill adults living in the community have a high risk for HIV infection. The purpose of this study was to identify risk knowledge, high-risk behaviors, and risk-related encounters of chronic psychiatric outpatients. **Method:** Detailed information on high-risk behaviors and risk-related situations during the past 12 months was collected from 60 outpatients appearing for regular visits at inner-city community mental health clinics. **Results:** Of the 60 outpatients, 37 (62%) had been sexually active during the past year, and 42% of the men and 19% of the women reported multiple sexual contacts and infrequent use of condoms during intercourse. Assessments of the patients' knowledge of AIDS risks revealed substantial deficits in their practical understanding of AIDS and risk reduction measures. Although use of intravenous drugs was uncommon in this group, many subjects reported histories of 1) trading sex for money, drugs, or a place to stay, 2) coercion to engage in unwanted sex, 3) casual sexual encounters, and 4) sexual activity after use of drugs or intoxicants. Twenty percent of the subjects had met their sexual partners on the streets, in parks, or in other public places. One-third had been treated for sexually transmitted diseases other than AIDS. **Conclusions:** These findings underscore the need for AIDS risk assessment, counseling, and prevention programs for the chronic mentally ill.*

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Cases of AIDS have been historically classified in terms of "risk groups," such as homosexual men and intravenous drug users. Although these categorizations are useful for surveillance purposes, overreliance on them can deflect attention from populations that are not traditionally considered high-risk groups but whose behaviors nonetheless place them at high risk for contracting HIV infection. One such population is the chronic mentally ill.

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Persons with chronic mental illness living in the community may be at higher than average risk for HIV infection for several reasons. While some individuals with severe psychopathology—especially those who are older, have major depressive disorders, or take psychotropic medications that reduce libido—have low rates of sexual interest or activity (1-3), clinical and descriptive studies have established associations between schizophrenia, bipolar illness, or borderline disorder and hypersexuality, indiscriminant sexual activity, or impulsive sexual behavior (4-9). Even the chronic mentally ill whose disorders are not strongly associated with impulsive or inappropriate sexual behaviors are likely to exhibit problem-solving, planning, and judgment deficits that increase vulnerability to casual, transient, coercive, or exploitative sexual relationships. Related to these characteristics is the difficulty many of the chronic mentally ill have in establishing stable social-sexual relationships and their frequent sharing of living quarters with, or proximity to, others who have similar

TABLE 1. Inaccurate Knowledge of AIDS Risk Behavior Among 60 Chronic Mentally Ill Subjects

True-False Question	Subjects Who Answered Incorrectly	
	N	%
Most people become sick quickly after getting the AIDS virus	32	53
Women can't get AIDS if they only have sex with men	26	43
People who can give you the AIDS virus always look sick	27	45
Men can't get AIDS if they only have sex with women	23	38
Washing after sex stops AIDS	23	38
Only gay (homosexual) men get AIDS	20	33
You must have many sex partners to get AIDS	19	32
Sex with someone who has used injected drugs creates risk for AIDS	17	28
Using condoms (rubbers) can help prevent AIDS	14	23
Unborn babies can get AIDS from their mothers	11	18
You can get the AIDS virus through one sexual contact	9	15

problems and also function marginally. Finally, the urban chronic mentally ill are often concentrated in inner-city neighborhoods with high rates of drug abuse, alcoholism, sexually transmitted disease, and HIV. Thus, the urban environment increases the HIV risk for the chronic mentally ill living in the community.

Over the past several years, a number of reports (3, 10–13) have stressed the need to better address AIDS prevention for psychiatric patient populations. However, to our knowledge there has been little research on risk behavior characteristics of the chronic mentally ill. Baer et al. (14) assessed psychiatric patients' understanding of AIDS risk and found that knowledge deficits were relatively common. In a larger-scale study, Sacks et al. (15) interviewed patients admitted to an acute psychiatric inpatient unit in New York City and found that 20% of the patients were at very high risk because they engaged in unprotected anal intercourse, needle sharing, or intercourse with HIV-infected partners, and a larger proportion reported multiple heterosexual partners. Approximately 6% of the subjects who were tested had positive HIV antibody results.

The purpose of the present study was to more closely investigate the AIDS risk characteristics of a group of chronic mentally ill adults living in the community. In addition to identifying risk knowledge and behaviors, we sought to obtain information on types of high-risk situations encountered by the chronic mentally ill. By identifying these risk characteristics, it will be possible to better develop education and prevention approaches for this population.

METHOD

The study was conducted in early 1991 in inner-city community mental health clinics in Wisconsin. The

population served is primarily urban, chronic mentally ill patients; nearly 70% have diagnoses of schizophrenia or other psychoses, and 85% have histories of prior psychiatric hospitalization. Patients between the ages of 18 and 47 years were recruited for study participation when they came to the clinics for regular follow-up appointments; almost all had primary clinical diagnoses of schizophrenia, affective disorder, or severe borderline personality. Sixty patients (about 80% of all approached) voluntarily participated in the assessment. The patients who did not participate either refused or were acutely psychotic and appeared unable to provide valid responses. Thirty-two were men and 28 were women. The mean age was 35.8 years ($SD=6.7$), the mean education level was 12.3 years ($SD=2.7$), 56 (93%) were unmarried, and 24 (40%) were white, 34 (57%) were African-American, and two (3%) were Hispanic. Thirty-four (57%) lived in apartments, 15 (25%) lived with their families, and the other 11 (18%) lived in boarding or group homes.

Each subject was individually and privately administered a questionnaire involving AIDS risk behavior, knowledge of AIDS risk, and several other risk characteristics. The questionnaire was presented in written form, and subjects with low reading and comprehension levels were assisted by a research staff member, who read the questions aloud, demonstrated how to complete each item, and clarified the meaning of the questions by using vernacular familiar to the subject. To promote candor, no identifying personal characteristics were collected. The assessment required about 30 minutes for most subjects to complete.

Eleven true-false items were used to measure the respondent's practical understanding of risk behavior and risk reduction steps. The scale items, shown in table 1, were adapted from those used in our prior intervention research (16) and previously normed and validated with other populations, including minority adults (17). The items used in the present study were those which tapped knowledge areas believed most pertinent to risk characteristics of this population.

Each subject was asked to report number of same- and different-sex partners, frequency of intercourse, and frequency of condom use in both the preceding 1-month and 12-month periods. The shorter interval was used to provide a brief retrospective sampling period less susceptible to recall error, and the longer period permitted the detection of low-frequency events that may not have occurred in the past month. Each subject also reported whether—in the past month and in the past year—alcohol, marijuana, crack, illicit injected drugs, or illicit pills were used.

To identify situational circumstances related to risk behavior in this population, each subject was asked to indicate whether, in both the preceding month and the past year, he or she had 1) had sex with someone to obtain money, drugs, or a place to stay, 2) had sex with a partner known less than 1 day, 3) had sex after drinking or drug use, 4) had sex with a partner who used intravenous drugs, 5) been pressured to engage in un-

TABLE 2. AIDS Risk Situations Encountered by 60 Chronic Mentally Ill Subjects in the Past Month and Past Year

Risk Situation	Patients Reporting Situation			
	Past Month		Past Year	
	N	%	N	%
Had sex in exchange for money, drugs, or a place to stay	7	12	8	13
Had sex with partner known for less than 1 day	3	5	6	10
Was pressured into unwanted sex	8	13	9	15
Had sex after using alcohol or drugs	9	15	12	20
Was receptive partner in anal intercourse	1	2	2	3
Had sex with a partner who used intravenous drugs	2	3	4	7

wanted sex, or 6) engaged in receptive anal intercourse. In addition, the subjects used a checklist form to indicate locations where they had met sexual partners in the past year.

All subjects were asked whether they ever had been treated for syphilis, gonorrhea, chlamydia, or genital herpes and whether they had been tested for HIV. If tested for HIV, the subject was asked to indicate whether the result was positive or negative. Each subject was asked to rate her or his personal concern about AIDS on a 5-point Likert scale (1=not at all concerned, 5=very concerned).

RESULTS

Knowledge of AIDS Risk Behaviors

Table 1 lists the questions regarding knowledge of AIDS risk behaviors and shows the proportion of subjects who incorrectly answered each question. In contrast to the high knowledge levels found in AIDS risk surveys of the general population (18), there were substantial deficits in risk knowledge among these chronic mentally ill persons. For example, 43% believed that heterosexual women cannot get AIDS and 45% believed that a person's appearance signals whether he or she has HIV infection. Particularly since the true-false format of the questions would yield a 50% correct rate through guessing alone, it is evident that many patients were substantively uninformed about practical aspects of HIV risk reduction.

Sexual Behavior and Substance Use

Of the 60 subjects, the percentages who said they had been sexually active in the past month and past year were 52% (N=31) and 62% (N=37), respectively. The proportions of men who reported they had had multiple sexual partners in the past month and year were 32% (N=10) and 42% (N=13), respectively. Men who were sexually active reported an average of 2.3 (SD=2.2) dif-

ferent female partners in the past month and 13.2 (SD=19.9) different female partners in the past 12 months. Eleven percent of the men who had female partners (N=2) said they also had had homosexual partners in the previous year. Over the preceding year, the men reported using condoms during an average of 18% of all instances of intercourse.

Fewer of the women in the group reported having had multiple partners during the past month and year: 12% (N=3) and 19% (N=5), respectively. However, these sexually active women reported an average of 3.0 (SD=2.9) different male partners in the past month. Condom use during intercourse was reported by few women; in only 12% of all instances of intercourse were condoms used.

Within the total group, in the past year alcohol had been used by 55% of the subjects (N=33), marijuana by 15% (N=9), crack cocaine by 8% (N=5), illicit drugs in pill form by 8% (N=5), and injected drugs by 5% (N=3). Similar proportions reported use of these substances in the past month: alcohol, 54% (N=32); marijuana, 12% (N=7); crack, 5% (N=3); illicit pills, 7% (N=4); intravenous drugs, 2% (N=1).

Risk Situations Encountered

Table 2 lists risk-producing situations and shows the proportions of subjects who reported encountering each in the past month and in the past year. Eighty-three percent of all subjects reported encountering at least one of these risk situations in the past year. Some risk situations were encountered in the past month almost as often as in the past year. When asked where they had met their sexual partners, 20% of the subjects (N=12) indicated that they had met their partners on the street, in parks, or in public places, 18% (N=11) had met them in bars, 10% (N=6) had met them at the mental health centers, and the balance had met their partners through other means, such as introductions by friends.

Sexually Transmitted Diseases, HIV Testing, and Concern About AIDS

Thirty-three percent of all subjects (N=20) reported that they had been diagnosed and treated for syphilis, gonorrhea, chlamydia, or genital herpes. Thus, a substantial number of patients had histories of treatment for sexually transmitted diseases, which is not unexpected in light of the data on their levels of sexual activity. Thirty-three percent also said they had been tested for HIV antibodies; none reported being told the test result was positive, although we do not know the circumstances under which these subjects were tested and we did not perform testing to establish HIV seroprevalence in this research. When asked to indicate personal concern about getting AIDS, 53% of the subjects (N=32) said they were "quite" or "very" concerned, and only 12% (N=7) said they had no concern.

DISCUSSION

The results of this study demonstrate alarmingly high rates of HIV risk behavior in a group of chronic mentally ill adults living in an urban community. Although some individuals were clearly at little risk—38% of the group reported neither sexual activity nor intravenous drug use in the past year—the majority of patients were sexually active, many had multiple sexual partners, and few regularly used condoms. The high frequency of multiple-partner contacts among sexually active men—an average of more than 13 female partners in the past year—was especially striking. For this reason, a history of sexually transmitted disease was also common.

Our findings with these chronic mentally ill patients living in the community confirm those recently reported by Sacks et al. (15) for acutely ill hospitalized psychiatric patients and further highlight several potential areas for preventive intervention. First, chronic psychiatric patients appear to have substantial deficits in practical AIDS risk knowledge that require educational efforts. Second, most patients reported encountering situations that led to high-risk behavior, such as sexual coercion by others, sexual activity after substance use, sexual activity with casual partners, or trading sex for money or a place to stay. These patterns may prove amenable to training in problem solving, assertiveness, and other skills and to other modes of intervention tailored to AIDS risk reduction. Such approaches have proven useful for teaching other types of "community survival" to the chronic mentally ill (19, 20) and also seem promising for AIDS prevention. Finally, these data clearly indicate that chronic psychiatric patients have a high potential vulnerability to HIV infection and argue for careful, routine clinical assessment of AIDS risk behavior in patients living in or being discharged to the community, the development and evaluation of AIDS prevention activities and their incorporation in the programs of both inpatient and outpatient mental health facilities, and consideration of offering HIV antibody counseling and testing to patients at high risk.

This study is preliminary in a number of respects, including its use of a relatively small number of subjects and reliance on self-reports of behavior and history of sexually transmitted diseases. Larger-scale studies are needed to further explore factors related to risk, to better establish the frequency of HIV and other sexually transmitted diseases in this population, and to test interventions aimed at behavior change. In future research it would be useful to examine differences in risk behavior in relation to patient gender and diagnosis in order to better tailor prevention counseling efforts. Growing evidence of the high-risk behaviors of chronic mentally ill persons, the increasing prevalence of HIV and other sexually transmitted diseases in the urban areas where many psychiatric patients live, and the cognitive, social, and emotional characteristics of

this population that increase their vulnerability make prevention efforts both challenging and urgently needed. Research evaluating the impact of individual, group, and community HIV risk reduction interventions for the chronic mentally ill is also now of great importance.

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Evidence of Dysfunction of a Prefrontal-Limbic Network in Schizophrenia: A Magnetic Resonance Imaging and Regional Cerebral Blood Flow Study of Discordant Monozygotic Twins

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***Objective:** The authors previously reported that in monozygotic twins discordant for schizophrenia the affected twin almost invariably had a smaller anterior pes hippocampus, measured with magnetic resonance imaging (MRI), and invariably had less regional cerebral blood flow (rCBF) in the dorsolateral prefrontal cortex during performance of the Wisconsin Card Sorting Test. The present study was an investigation of the relationship between hippocampal pathology and prefrontal hypofunction in the same twin pairs. **Method:** Nine pairs of monozygotic twins discordant for schizophrenia underwent MRI scanning for determination of anterior hippocampal volume and xenon-inhalation rCBF testing for determination of prefrontal physiological activation associated with the Wisconsin Card Sorting Test. **Results:** The differences within twin pairs on the MRI and rCBF measures were strongly and selectively correlated. Specifically, the more an affected twin differed from the unaffected twin in left hippocampal volume, the more they differed in prefrontal physiological activation during the Wisconsin Card Sorting Test. In the affected twins as a group, prefrontal activation was strongly related to both left and right hippocampal volume. These relationships were not found in the group of unaffected twins. **Conclusions:** This finding is consistent with the notion that schizophrenia involves pathology of and dysfunction within a widely distributed neocortical-limbic neural network that has been implicated in, among other activities, the performance of cognitive tasks requiring working memory.*

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It is increasingly appreciated that schizophrenia is associated with deficits in various cognitive functions, especially attention, memory, and "executive" functions (1). Although the mechanisms underlying these deficits are uncertain, recent speculation has focused on dysfunction of temporal-limbic and prefrontal brain regions as explanations for at least the deficits in memory and executive functions, respectively. Poor performance on prefrontal-type executive tasks, such as the Wisconsin Card Sorting Test, has been directly linked to physiological hypofunction of the prefrontal cortex in patients with schizophrenia (2-7), and subtle anatomical deviations in anteriomedial temporal lobe

structures implicated in memory processing have been interpreted as a pathological correlate of the impairments on memory tests also manifested by these patients (8-11). Furthermore, our group has reported data suggesting that these neurobiological findings might be related (12), and we have speculated that the heart of the matter is dysfunctional neocortical-limbic connectivity (12-15).

In a recent investigation of sets of monozygotic twins discordant for schizophrenia, we found that the affected twin almost invariably performed worse on memory tests (8) and on the Wisconsin Card Sorting Test (7, 8) than did the unaffected sibling. Moreover, we also found that the affected twin almost invariably had a smaller anterior pes hippocampus (16) and invariably had diminished relative prefrontal activity as reflected in a measure of regional cerebral blood flow (rCBF) during performance of the Wisconsin Card Sorting Test (7). In this investigation we examined the relationship between these putative abnormalities in hippocampal anatomy and prefrontal cortical physiology in this group of monozygotic twins in an effort to test

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directly the hypothesis of a dysfunctional neocortical-
limbic network.

METHOD

Subjects

The study group consisted of nine pairs of monozygotic twins discordant for schizophrenia who were recruited as part of a multidimensional study of schizophrenia in monozygotic twins. These nine pairs are all of the discordant twin pairs who had undergone both magnetic resonance imaging (MRI) and rCBF measurement. Characteristics of these twin pairs were described in detail previously (7, 8, 16). In brief, monozygosity was confirmed by analysis of 19 RBC antigens. Psychiatric diagnosis was established by structured diagnostic interview (SCID parts I and II [17]). The affected member of each twin pair fulfilled the *DSM-III-R* criteria for chronic schizophrenia, and the unaffected member had no evidence of major psychopathology and did not fulfill criteria for an axis I psychiatric disorder. Three pairs were women, and six pairs were men; their mean age was 32 years (range, 25–44 years). Each twin pair had been discordant for at least 4 years when the study began and had remained discordant for an additional 3-year follow-up period. The affected twins were all taking antipsychotic medications at the time of the study. They were in excellent general medical health and had no sign of dehydration or malnutrition. They had been screened for major medical problems and for history of noteworthy drug abuse, head trauma, and other neurological problems. The results of rCBF measurements of this group have been reported in detail elsewhere (7). The MRI scans of these subjects were part of a study of a larger group of monozygotic twins discordant for schizophrenia, and the anatomical measurements from the MRI scans have also been reported previously (16).

Magnetic Resonance Imaging

The method for making anatomical measurements from MRI scans has been described in detail elsewhere (16). In brief, we used spin-echo coronal sections weighted for T_1 relaxation time (repetition time=800 msec, echo time=20 msec); the sections were 5-mm-thick contiguous slices parallel to the floor of the fourth ventricle and were acquired with the same 1.5-tesla magnet (General Electric Signa) for each of the subjects. We used an interactive method for outlining structures of interest on digitized images displayed on a computer image analysis system. In the prior anatomical study (16), the volume of the anterior pes hippocampus was the most robust discriminator of affected from unaffected twin and was selected a priori as the anatomical measure of interest for this investigation. This measure was determined by summing the areas of the pes hippocampus in the first four slices posterior to the amygdala, including a slice through the amygdala-hippocam-

pus junction. The volumes of the pes hippocampus on both the right and left sides were determined. To include a hypothetically "neutral" MRI measure (i.e., a measure that did not discriminate affected from unaffected twin), we derived cerebral volume by adding the total cerebral areas in the four slices through the anterior hippocampus. The raw data concerning these measures have been given elsewhere (16).

Regional Cerebral Blood Flow

The method for determining rCBF by xenon inhalation has also been described in detail elsewhere (2, 4, 7). In brief, the procedure involved a 60-second inhalation of a mixture of xenon-133 gas and air followed by 14 minutes of "washout," during which only room air was inhaled. Regional cerebral blood flow was calculated (by using a biexponential model for gray and white matter compartments) from the radioactivity desaturation curves generated by 32 extracranial gamma ray detectors. Each subject underwent three consecutive rCBF procedures separated by approximately 30 minutes and carried out under three different testing conditions. The first measurement was made during an eyes-closed resting condition that served to acclimate the subjects to the testing procedure. The second and third conditions were an automated version of the Wisconsin Card Sorting Test and a simple sensorimotor control task. They were presented in counterbalanced sequence to control for the possibility of an order effect. The control task was designed to serve as a nonspecific sensorimotor baseline activation condition so that rCBF during the Wisconsin Card Sorting Test could be compared with a control value (2). We calculated rCBF as the initial slope, a unitless measure of cortical gray matter perfusion (18). Initial slope values from 32 cortical regions were collapsed into five regions, as previously described (2, 4, 7). The raw rCBF data have been given elsewhere (7).

Statistical Analysis

The purpose of this study was to examine the relationship between anatomical differences in the volume of the pes hippocampus and physiological differences in prefrontal activation during the Wisconsin Card Sorting Test within monozygotic pairs discordant for schizophrenia. To achieve this goal, we selected two measures a priori as those most likely to test the presence of a relationship.

1. For each twin pair an anatomical difference value was computed by subtracting the pes hippocampal volume in the affected twin from the same measure in the unaffected twin. If we assume that the unaffected twin is an ideal subject for comparison with the affected twin in each pair, the within-pair anatomical difference can be taken as a measure of the relative extent of the putative anatomical pathology associated with schizophrenia in the affected twin.

2. For each pair we computed the difference in rCBF activation associated with the Wisconsin Card Sorting

TABLE 1. Within-Pair Differences in MRI Anatomical Measures for Monozygotic Twins Discordant for Schizophrenia

Twin Pair	Age (years)	Sex	Within-Pair Difference in Volume (cm ³) ^a		
			Left Hippocampus	Right Hippocampus	Cerebral Volume Measure
1	38	F	0.35	0.14	-0.6
2	38	F	0.06	-0.02	-5.2
3	33	M	0.14	0.16	-2.2
4	31	F	0.16	0.20	-8.5
5	25	M	0.24	0.01	-4.3
6	28	M	0.35	0.76	11.0
7	44	M	0.36	0.29	-0.7
8	28	M	0.24	0.08	4.9
9	27	M	0.03	0.13	-1.9

^aVolume in affected twin was subtracted from volume in unaffected twin.

Test. First, each individual's rCBF *activation* related to performance of the Wisconsin Card Sorting Test was determined. This was accomplished by subtracting the rCBF data during the control task from the rCBF data during the Wisconsin Card Sorting Test. This "subtraction" method has become widely accepted as the "gold standard" for isolating behavior-specific regional brain activity during rCBF studies (2, 19). Second, this difference in rCBF "activation" for the affected twin was subtracted from the analogous value for the unaffected twin. This within-pair physiological difference can be taken as a measure of the relative extent of the cognition-linked dorsolateral prefrontal cortical hypofunction in the affected twin.

The correlation of these within-pair differences in left and right pes hippocampal volumes and within-pair differences in rCBF activation was examined by several procedures, both parametric and nonparametric. Simple nonparametric correlations were performed with the Spearman rho test. Because cerebral perfusion is highly intercorrelated across brain regions and the majority of the variance in regional perfusion is accounted for by the level of global brain perfusion (20), correlations, if found, may not reflect an anatomical relationship with cortical neuronal activity that is *uniquely* regional. Alternatively, such correlations may be obscured by the "noise" introduced by global perfusion variance. To account for these possibilities, we performed a partial correlation procedure to address the principal theoretical question of this study, namely, whether and to what extent the MRI data relate to rCBF data (and, by inference, neuronal activity) that are uniquely regional (i.e., not accounted for by whole brain CBF). This approach is analogous to other methods, such as analyses of covariance (20), that attempt to highlight local brain activity by adjusting regional data for the level of global flow, but the partial correlation approach addresses the strength of the relationship between variables rather than differences in means. The procedure involved using linear regression to remove the effect of the differences in whole brain CBF on the

TABLE 2. Within-Pair Differences in rCBF Activation During the Wisconsin Card Sorting Test for Monozygotic Twins Discordant for Schizophrenia

Twin Pair	Within-Pair Difference in rCBF Activation ^a					
	Prefrontal	Central	Temporal	Parietal	Parieto-Occipital	Whole Brain
1	23.4	10.7	8.6	4.0	5.8	10.5
2	-7.2	-5.7	-4.8	-4.3	2.1	-4.5
3	1.7	0.1	-0.1	-0.5	-1.8	-0.7
4	-10.2	-7.8	-2.3	-7.6	-9.3	-8.2
5	4.3	4.0	-6.2	2.9	-4.7	1.9
6	12.9	10.1	-2.3	8.7	7.7	10.3
7	19.6	8.8	7.9	10.5	11.2	11.5
8	-8.8	-9.2	-4.9	-8.8	-6.9	-8.2
9	4.0	-11.5	-9.4	-9.5	-11.4	-8.6

^aRegional cerebral blood flow during a control task was subtracted from rCBF during the Wisconsin Card Sorting Test. The difference value for the affected twin was subtracted from the difference for the unaffected twin. The values shown here are (unitless) initial slope values from 32 cortical regions collapsed into five regions; the raw data have been given elsewhere (7).

regional differences and correlating the residuals with the MRI difference data. This procedure is referred to as a "semipartial correlation" (21). Because of the relatively small number of subjects, the residual rCBF differences and the MRI differences were also subjected to a nonparametric Spearman correlational analysis. The statistical procedures were performed on a mainframe computer with Statistical Analysis System programs (SAS Institute, Cary, N.C.).

RESULTS

The twin pairs' age, sex, and within-pair differences in the anatomical measures are shown in table 1. The within-pair differences in rCBF activation during the Wisconsin Card Sorting Test are shown in table 2. Left hippocampal anatomical differences and rCBF differences correlated for each region (in all cases, $\rho > 0.7$, $p < 0.05$) and for the whole brain ($\rho = 0.82$, $p < 0.01$). No significant rCBF correlations emerged for right hippocampal differences (in all cases, $\rho > 0.15$). As expected, rCBF differences were highly correlated between all regions and with mean whole brain CBF (in all cases, $\rho > 0.90$, $p < 0.001$). Therefore, to statistically remove the variance in rCBF that is accounted for by whole brain blood flow, the partial correlation procedure was performed. With the correlation between the regional perfusion differences and whole brain perfusion differences thus statistically partialled out, only the dorsolateral prefrontal cortical rCBF differences and the left pes hippocampus volume differences remained significantly positively correlated, according to both the parametric and nonparametric analyses (table 3 and figure 1). This correlation suggests that more hippocampal pathology is associated with less prefrontal activation and that almost two-thirds of the residual variation in prefrontal activation is accounted for by this relationship. Nearly significant negative correla-

TABLE 3. Correlations of Within-Pair Differences in Anterior Hippocampal Volume and Residual rCBF Activation During the Wisconsin Card Sorting Test for Monozygotic Twins Discordant for Schizophrenia

Cortical Region	Correlation of Within-Pair Difference in Residual Cortical rCBF Activation and Within-Pair Difference in Hippocampal Volume							
	Left Hippocampus				Right Hippocampus			
	Spearman		Pearson ^a		Spearman		Pearson ^a	
	Rho	p	r	p	Rho	p	r	p
Prefrontal	0.80	<0.01	0.82	<0.01	0.07	>0.80	0.31	>0.40
Precentral	-0.43	<0.24	-0.49	>0.18	-0.40	>0.20	0.13	>0.70
Temporal	-0.02	>0.90	0.04	>0.90	0.33	>0.30	-0.19	>0.60
Parietal	-0.63	<0.08	-0.71	<0.04	-0.60	<0.09	0.44	>0.20
Parietal-occipital	-0.30	>0.43	-0.29	>0.40	0.10	>0.70	-0.35	>0.30

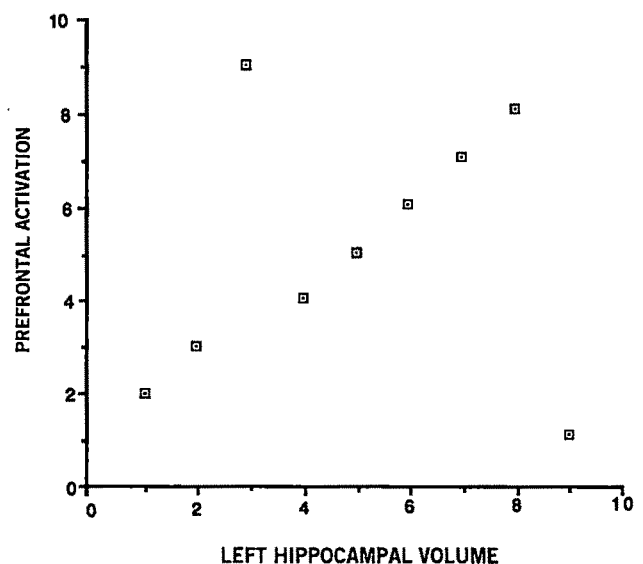
^adf=7.

tions were found for both left and right hippocampus and residual parietal flow. This correlation suggests that more hippocampal pathology is associated with greater parietal activation. The results of a test for a relationship between within-pair differences in the cerebral volume measure and residual prefrontal rCBF activation were not significant (Spearman $\rho=0.40$, $p=0.29$; Pearson $r=0.26$, $p=0.50$).

Post hoc correlations were performed to address whether the results depended on the presence of illness per se. In the unaffected twins as a group, there were no significant correlations between pes hippocampal volume and rCBF activation during the Wisconsin Card Sorting Test, either without or with partial correlations ($p>0.2$ in each case). In the affected group, after the partial correlation procedure was performed prefrontal activation correlated strongly with both the left ($\rho=0.75$, $p=0.02$) and right ($\rho=0.82$, $p<0.01$) hippocampus volumes (figure 2), parietal activation correlated inversely with left ($\rho=-0.68$, $p<0.05$) and right ($\rho=-0.65$, $p<0.06$) hippocampus volumes, and no other correlations, including those without partial correlations, approached significance ($p>0.3$ in all cases).

DISCUSSION

In this study of identical twins discordant for schizophrenia, we found that the magnitude of the within-pair difference in the volume of the left anterior pes hippocampus strongly predicted the difference within the same pair in physiological activation of the dorsolateral prefrontal cortex during a cognitive task that normally elicits physiological activation of this prefrontal brain region (2, 4, 6, 22). Specifically, the smaller the hippocampal volume of the affected twin relative to his or her co-twin, the less activation of the dorsolateral prefrontal cortex during performance of the Wisconsin Card Sorting Test. If the unaffected twin in each pair can be regarded as defining "normality" for that pair on each of the experimental measures, then an anatomical "abnormality" of the pes hippocampus is associated with a cognitively linked physiological "abnormality" of the dorsolateral prefrontal cortex in the affected

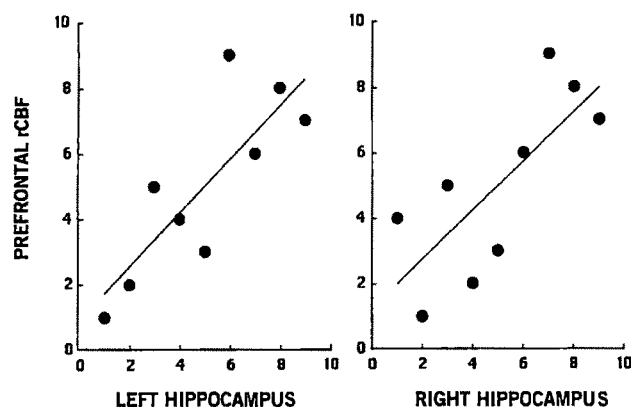
FIGURE 1. Relation of Within-Pair Difference in Left Hippocampal Volume to Difference in Prefrontal rCBF Activation for Monozygotic Twins Discordant for Schizophrenia^a

^aActivation of rCBF was measured during the Wisconsin Card Sorting Test; whole brain CBF was partialled out. Values represent rank ordering for each variable. Spearman $\rho=0.80$, $p<0.01$.

twin. If the affected twins have the same neurobiological illness as nontwins with schizophrenia, and there is no compelling body of data to indicate the contrary, then this finding adds to the growing body of evidence implicating dysfunction of neocortical-limbic connectivity in patients with this illness.

Although it is tempting to infer a mechanistic relationship from the correlations found in this report (e.g., hippocampal pathology disrupts prefrontal function), such a conclusion is purely speculative and must be viewed with caution. It is possible that the correlation is a reflection of something that affects both the hippocampus and prefrontal cortex independently but in a functionally related manner. For example, there may be pathological changes, either primary or secondary to the illness, in both brain regions, the effects of which

FIGURE 2. Rank Order Correlation Between Hippocampal Volume and Prefrontal rCBF Activation in Affected Monozygotic Twins With Schizophrenia^a



^aActivation of rCBF was measured during the Wisconsin Card Sorting Test; whole brain CBF was partialled out. Values represent rank ordering for each variable. Left hippocampus: Spearman $\rho=0.75$, $p<0.02$; right hippocampus: Spearman $\rho=0.82$, $p<0.01$.

are most apparent when conjoined function from these regions is required. In other words, prefrontal dysfunction may not be a reflection of defective communication with the anteriomedial temporal lobe but a reflection of intrinsic prefrontal pathology. This possibility cannot be excluded. The impact of medication on the affected twin also cannot be ruled out, but this seems an unlikely explanation for the cognitively and regionally specific relationships we found (3, 7, 23).

Regardless of the precise mechanism, the correlations suggest dysfunction within a widely distributed neural network that has been shown in nonhuman primates to be involved in the performance of "working memory" tasks that are analogous in many ways to the Wisconsin Card Sorting Test (24). Goldman-Rakic and Friedman (25) recently used the 2-deoxyglucose autoradiographic technique with rhesus monkeys to demonstrate that performance of working memory tasks results in metabolic activation and coupling of a distributed network comprising the anterior hippocampus, ventral anterior and dorsomedial thalamus, parietal cortex, and dorsolateral prefrontal cortex. Lesion studies (26, 27) and electrophysiological studies (28) of these regions in the monkey have also suggested that they participate as a neural ensemble in the performance of such cognitive tasks. The fact that the anterior hippocampus and dorsolateral prefrontal cortex may normally communicate with each other during the performance of such tasks implies that a defect in one part of this network (e.g., an anatomical deviation in the temporal-limbic component) might have functional implications throughout the network. The results of the present study are consistent with this possibility. The assumptions that the impairment is of a behavior-specific neural network and is associated with schizophrenia per se are supported by several aspects of this study, including the facts that the correlation held only for the activation

associated with the Wisconsin Card Sorting Test and that it was not found in the unaffected twins as a group.

Because of the methodological limitations in our rCBF technique, especially its inability to measure activity beyond the dorsal cortical surface, we were not able to study rCBF in other components of the putative network (e.g., thalamus, limbic cortex). It is interesting, however, that measures of physiological activity in cortical areas not part of the putative network (i.e., lateral temporal, precentral, and parieto-occipital cortices) were not uniquely correlated with the hippocampal anatomical abnormality. By the same token, an anatomical measure not part of the putative network did not predict rCBF within the network. These negative results further attest to the anatomical specificity of the neural systems involved. Although it is doubtful that the dorsolateral prefrontal cortex and anterior hippocampus are functionally coupled only during working memory or that dysfunction of this neural network in schizophrenia affects only working memory, performance of working memory tasks such as the Wisconsin Card Sorting Test appears to be a sensitive probe of the functional integrity of this network in this illness (15, 22).

In addition to a direct correlation of apparent temporal-limbic pathology with malfunction of the dorsolateral prefrontal cortex, an inverse correlation was also found with regional activation of the parietal cortex. This finding is consistent with the data from nonhuman primates implicating the parietal cortex as an important component of the network (25), at least to the extent that the parietal cortex was the only other cortical region that showed a nearly significant correlation with the hippocampal abnormality. However, the fact that the correlation was in the opposite direction from the correlation with the dorsolateral prefrontal cortex is difficult to interpret. It may suggest, as proposed by Mesulam (29), that prefrontal activation inhibits parietal function. We have found some evidence to support this proposal in studies of rCBF during the Wisconsin Card Sorting Test in normal subjects (22) and in some patient groups (30), where prefrontal and parietal cortex activation may be inversely related. However, the data on metabolic activation during working memory tasks in monkeys show increased metabolism in the parietal cortex (25), a finding that might be expected even if the region were inhibited, because inhibitory synaptic activity may be metabolically demanding. This apparent inconsistency notwithstanding, the finding that greater hippocampal pathology relates to greater parietal physiological activation in these patients misses the possibility that while the network may be underactivated prefrontally, it may also be intrinsically disorganized.

The results in this investigation are also consistent with the findings in an earlier study from our group that used a less sensitive anatomical method. We previously reported (12) that cerebral ventricular size on CT scans, a measure that has been found in numerous studies to be greater than normal in patients with schizophrenia (31), also predicted prefrontal rCBF during the Wisconsin Card Sorting Test but not during another task that

did not require working memory. Although the reason for large ventricles in schizophrenia is uncertain, it has been shown in some studies to be correlated with small hippocampal volume (32).

It should be noted that the anatomical component of almost all of the correlations of within-pair differences involved the left hemisphere. The interpretation of this apparent lateralization of the anatomical-physiological correlation is not straightforward. It may mean that dysfunction of the implicated neural network is lateralized, perhaps on the basis of lateralized neuropathology (33). While the neuropathological abnormalities in the brain in schizophrenia are usually bilateral (34), unilateral abnormalities have been reported and typically favor the left hemisphere (33). An alternative explanation for the lateralized correlation in our study is that the Wisconsin Card Sorting Test may have a bias toward activation of the left hemisphere (6, 35) and thus did not recruit (i.e., test) to the same degree the homologous network in the right hemisphere. In the studies of Milner (36) on the effect of cerebral lesions on performance on the Wisconsin Card Sorting Test, left hemisphere insults tended to have a greater effect. The possibility also cannot be excluded that examining the within-pair differences somehow exaggerated an apparent laterality effect. When the data of the affected twins were analyzed separately, the correlations were bilateral. These questions clearly require further investigation and cannot be answered at the present time.

In a previous study (4) we proposed that a possible mechanism of prefrontal hypofunction during the Wisconsin Card Sorting Test in patients with schizophrenia might involve dysfunctional dopaminergic afferentation of the dorsolateral prefrontal cortex. This proposal was based on the finding in a group of patients with schizophrenia of a positive correlation between prefrontal rCBF during the Wisconsin Card Sorting Test and CSF concentrations of homovanillic acid (4), on similar physiology-behavior relationships in patients with Parkinson's disease (37), and on data from nonhuman primates linking prefrontal dopaminergic function to performance on working memory tasks (38, 39). In light of the present report and the suggestion that prefrontal hypofunction during the Wisconsin Card Sorting Test may reflect dysfunction of a wider neural network, a revision of the earlier proposal may be in order. Since there are no dopaminergic pathways that directly (i.e., monosynaptically) link components of the implicated neural system, it is more likely that if dopaminergic function is affected, it is a secondary phenomenon. There are at least two potential mechanisms for this. Anatomical tracing studies in the rat indicate that prefrontal, probably glutamatergic, projection neurons form synapses with midbrain dopaminergic neurons that project back to the prefrontal cortex (40, 41). This finding suggests that the prefrontal cortex can monosynaptically regulate its own dopaminergic afferentation, perhaps as a means of enhancing or focusing cortical activity when it is particularly advantageous to do

so (42). If the prefrontal cortex is hypoactive because of a primary failure of activation of the prefrontal-limbic network, a secondary effect of this hypoactivity might be diminished excitation of dopaminergic afferents from the ventral tegmental area. In other words, if cortical dopaminergic afferent activity is dysfunctional in schizophrenia, it may be a result, not a cause, of prefrontal hypoactivity. An alternative possibility may involve direct glutamatergic projections from anterior hippocampus to dopaminergic neurons in the ventral tegmental area (43). It is conceivable that loss of function in these excitatory projections may be an additional basis for prefrontal dopaminergic afferent hypoactivity. Preliminary studies of temporal-limbic lesions in the rat support these mechanistic explanations (44, 45). By either mechanism, prefrontal dopaminergic dysfunction, although a secondary, rather than primary, pathophysiological condition could still have important implications for prefrontal function (38, 39, 42).

Throughout this century, the study of monozygotic twins discordant for schizophrenia has been a powerful approach to highlighting biological aspects of this illness. For example, data from monozygotic twin studies have established the importance of both genetic and environmental factors in the pathogenesis of schizophrenia. In an earlier twin study, Reveley et al. (46) showed with CT scans that the ventricles of affected twins were larger than those of unaffected twins. In our series of monozygotic twin studies, this approach has enabled us to observe subtle cognitive (8) and anatomical (16) differences within pairs that almost invariably discriminated the affected from the unaffected twin and physiological differences (7) that thus far have invariably made this discrimination. Because of the subtle differences within pairs in each of these measures and the considerable variability found in the normal population on these measures, it is not surprising that such a high degree of discrimination has not been found in studies of nontwin subjects. By the same token, the correlation reported here between a small reduction in size of the anterior hippocampus measured on an MRI scan and a slight diminution in rCBF related to a specific cognitive task may not be found in other groups unless very large numbers of subjects are studied. If this prediction is correct, it raises the question of whether the correlation itself is so rarefied as to be neurobiologically trivial. This possibility can be explored in future studies that address in other ways the integrity of prefrontal-temporal-limbic connectivity. In the meantime, the finding of a statistically strong correlation between abnormal hippocampal morphology and abnormal prefrontal physiology that is in the hypothesized direction (i.e., more abnormality of one predicting more abnormality of the other) and its emergence under very specific conditions (i.e., when both the effect of illness is amplified by a within-pair comparison and the relevant neural system is stressed by a cognitive task that demands function from it) implicate by direct experimental evidence dysfunction of this neural connectivity in the pathophysiology of schizophrenia (47).

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Neuropsychological Functioning of First-Episode Schizophreniform Patients

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***Objective and Method:** This study compared 32 consecutively admitted first-episode schizophreniform patients, 26 patients with chronic schizophrenia according to the DSM-III-R criteria, and 25 normal comparison subjects on a comprehensive battery of neuropsychological tests to determine the degree of cognitive impairment existing at the onset of schizophrenic illness. Patients were tested within 2 weeks of admission to the hospital, after their medication had been stabilized. **Results:** With age and education controlled, the first-episode and chronic patients performed significantly worse than the normal subjects on neuropsychological summary measures of executive function, verbal memory, spatial memory, concentration/speed, and global cognitive function and on left and right hemisphere function scales. The first-episode patients were as cognitively impaired as the chronic patients on all summary scales and many of the individual tests. Both groups showed relatively greater left than right hemisphere dysfunction. **Conclusions:** These findings suggest that substantial cognitive deficits, comparable to those of chronic patients, are present early in the course of psychotic illness.*

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Neuropsychological research focusing on cognitive deficits in schizophrenia has resulted in several important yet potentially contradictory findings. Studies have shown that chronic patients demonstrate a diffuse pattern of cognitive impairment which is frequently indistinguishable from that of brain-damaged patients (1-3). Some reports have suggested that there is a focal pattern of deficit, such as left hemisphere dysfunction (4-7), frontal lobe impairment (8-10), or dysfunction of the temporal-limbic cortex (8, 11). All of these investigations have included heterogeneous groups of chronic patients at different stages in the course of their illness, with varying histories of medication and numbers of hospitalizations.

Studies of military inductees (12, 13) confirmed that there was a deterioration in cognitive function from premorbid levels (at the time they enlisted in the service) to the onset of illness; however, these patients had al-

ready been diagnosed as schizophrenic for 2-11 years when they were tested after the onset of illness. Longitudinal neuropsychological studies of schizophrenic patients (reviewed by Heaton and Dr  xler [14]), in which testing was done after the onset of illness and at follow-up intervals, have indicated either no change or modest improvement on measures of cognitive function, particularly in patients with a good clinical outcome. A subgroup of chronically hospitalized patients seem to show cognitive deterioration when retested. In most of these studies, patients were tested early in their illness, but not necessarily in their first episode, and at various follow-up intervals. They were also given a limited number of cognitive tests.

Because of these limitations, it is unclear what degree of cognitive dysfunction exists at the onset of schizophrenic illness. This study was designed to determine whether schizophreniform patients would perform worse than normal subjects on many cognitive tasks and, if so, whether their deficits were comparable to those seen in chronic patients.

METHOD

The subjects included 32 first-episode psychotic patients (26 male and six female) consecutively admitted to a university-affiliated state hospital research unit with the *DSM-III-R* diagnosis of schizophreniform disorder (less than 6 months' duration). An additional 26 pa-

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TABLE 1. Characteristics of First-Episode Schizophreniform Patients, Chronic Schizophrenic Patients, and Normal Comparison Subjects Tested on Neuropsychological Functioning

Variable	First-Episode Schizophreniform Patients (N=32) (A)		Chronic Schizophrenic Patients (N=26) (B)		Normal Comparison Subjects (N=25) (C)		ANOVA		
	Mean	SD	Mean	SD	Mean	SD	F	df	p
Age (years)	26.1	6.5	31.1	8.5	26.1	6.0	4.4	2, 80	0.01 ^a
Education (years)	12.4	3.0	13.0	2.0	14.6	2.1	5.8	2, 80	0.004 ^b
Number of previous hospitalizations	0.0	0.0	5.3	8.1					
Age at first hospitalization (years)	26.1	6.5	24.6	8.0			0.4	1, 56	n.s.
Score on Scale for Assessment of Negative Symptoms ^c	18.7	15.9	32.8	21.4					
Score on Scale for Assessment of Positive Symptoms	22.4	17.6	27.6	23.1					

^aSignificant difference between A and B ($p < 0.05$, post hoc Tukey test) and significant difference between B and C ($p < 0.05$, post hoc Tukey test).

^bSignificant difference between A and C ($p < 0.05$, post hoc Tukey test).

^cSignificant difference between A and B ($t = -2.5$, $df = 1$, $p < 0.01$).

tients (16 male and 10 female) with the *DSM-III-R* diagnosis of chronic schizophrenia (12 undifferentiated type, eight paranoid type, four schizoaffective, and two disorganized type) constituted the chronic group. They included consecutive admissions to the same inpatient unit ($N = 17$) and all of the patients from the university day hospital program in the department of psychiatry ($N = 7$) and the outpatient department ($N = 2$) who were available during the time period of this study. The mean duration of illness, defined as the length of time since the first hospitalization, was 6.8 years ($SD = 7.6$; range = 2–31 years). All patients were receiving standard neuroleptic medications at the time of testing. Patients were excluded if they had histories of epilepsy, head injury with significant loss of consciousness, or other known neurological conditions.

The 25 normal comparison subjects (16 male and nine female) were randomly selected individuals who were approached while they were sitting in the lobby of the university hospital, a general medical facility providing health care for the county from which the patients were drawn. This group consisted of nonpsychiatric outpatients at the hospital ($N = 8$), hospital workers ($N = 5$), and patients' visitors ($N = 12$).

Characteristics of the three groups are shown in table 1.

Within the first 2 weeks after admission, all patients were interviewed with the modified Schedule for Affective Disorders and Schizophrenia—Lifetime Version (SADS-L) (15), and clinical ratings were assigned by a trained psychiatrist using the Scale for the Assessment of Negative Symptoms (16) and the Scale for the Assessment of Positive Symptoms (17). A final diagnosis was made by one of the authors (L.E.D.), who used information from the interviews, medical records, clinicians' observations, and family members. The normal comparison subjects were screened with the SADS-L and the Structured Interview for DSM-III Personality Disorders (18) by a trained interviewer. No individual who received a diagnosis of a major psychiatric or personality disorder was included in the normal group.

All of the inpatients were tested approximately 2 weeks after admission, after being stabilized on medication regimens. Outpatients and day hospital patients ($N = 9$) were tested during the course of their treatment, but not necessarily within 2 weeks of admission to their program. All subjects received a neuropsychological test battery, which included the following tests (19).

1. The measures of language function were the Pro-rated Verbal IQ, the standard score on the Reading subtest of the Wide Range Achievement Test, the Boston Naming Test, the Controlled Oral Word Association Test, and the Word Attack subtest of the Woodcock Reading Mastery Test.

2. The measures of executive/frontal function were the Wisconsin Card Sorting Test, the Booklet Categories Test (abbreviated form, subtests I–IV and VI), and the Stroop Color-Word Test. The Wisconsin Card Sorting Test is thought to be sensitive to dysfunction in the dorsolateral prefrontal cortex (10).

3. The measures of verbal memory included the Logical Memory and Associate Learning subtests of the Wechsler Memory Scale and the California Verbal Learning Test. Verbal memory has been associated with left temporal lobe function (20).

4. The measures of spatial memory were the Visual Reproduction section of the Wechsler Memory Scale and the Benton Visual Retention Test. Visual/spatial memory has been associated with right temporal cortical function (20).

5. The tests thought to reflect global cortical function, as well as overall concentration and motor speed, were the Trail Making Test (parts A and B), the Symbol Digit Modalities Test, the Cancellation Test, and the Finger Tapping Test.

6. Measures of finger agnosia and graphesthesia were given to assess sensory/perceptual function.

7. The Ravens Coloured Progressive Matrices (Ravens IQ) was administered to measure visual/perceptual capacity.

Scores on the Scale for the Assessment of Negative Symptoms and the Scale for the Assessment of Positive

TABLE 2. Standardized z Scores on Summary Scales of Neuropsychological Functioning for First-Episode Schizophreniform Patients, Chronic Schizophrenic Patients, and Normal Comparison Subjects

Summary Function Scale	First-Episode Schizophreniform Patients (N=32) (A)			Chronic Schizophrenic Patients (N=26) (B)			Normal Comparison Subjects (N=25) (C)			ANCOVA	
	Mean	SD	Adjusted Mean	Mean	SD	Adjusted Mean	Mean	SD	Adjusted Mean	F (df=2, 78)	p
Language	-0.98	1.27	-0.80	-1.07	0.93	-0.99	-0.00	0.74	-0.26	3.76	0.03 ^a
Executive	-1.09	1.00	-1.08	-1.22	1.29	-1.08	0.00	0.51	-0.14	7.20	0.001 ^b
Verbal memory	-1.23	1.03	-1.16	-1.28	1.15	-1.17	0.00	0.72	-0.19	8.00	0.0007 ^b
Spatial memory	-1.22	1.05	-1.19	-1.60	1.12	-1.45	0.00	0.69	-0.19	11.59	0.00004 ^b
Concentration/speed	-1.12	0.83	-1.07	-1.53	1.18	-1.42	-0.02	0.70	-0.19	11.35	0.00005 ^b
Sensory/perceptual	-0.45	1.00	-0.40	-0.47	1.00	-0.39	0.00	0.64	-0.11	0.75	n.s.
Global	-1.02	0.63	-0.95	-1.20	0.91	-1.08	-0.00	0.50	-0.17	13.18	0.00001 ^b
Left hemisphere	-1.04	0.73	-0.92	-1.14	0.91	-1.09	0.00	0.50	-0.17	11.93	0.00001 ^b
Right hemisphere	-0.59	0.61	-0.56	-0.61	0.78	-0.53	0.00	0.44	-0.11	3.94	0.02 ^b

^aSignificant difference between B and C ($p < 0.05$, post hoc Tukey test).

^bSignificant difference between A and C ($p < 0.05$, post hoc Tukey test) and significant difference between B and C ($p < 0.05$, post hoc Tukey test).

Symptoms were composite scores, or the sums of all individual items in each category.

Because of the large number of variables generated, summary scales for each function—language, executive, verbal memory, spatial memory, concentration/speed, and sensory/perceptual—were constructed, as well as a global scale, which was the average of the other scale scores. A left hemisphere and a right hemisphere scale were also constructed from the tests purported to reflect lateralized function. For the left hemisphere scale, language function, verbal memory, and right-handed sensory/perceptual and motor test scores were summed and averaged. For the right hemisphere scale, the Ravens IQ score, measures of visual/spatial memory, and left-handed test scores were similarly combined. Standardized z scores based on the mean scores and standard deviations of the normal comparison group were summed and averaged for each function. Internal reliability for the first six scales was good, with coefficient alphas ranging from 0.67 to 0.87. (An expanded explanation of the construction of the scales may be obtained from the first author on request.)

To evaluate the possibility that the acuteness of the psychosis might obscure differences between groups, 16 inpatients (eight schizophreniform, three chronic schizophrenic, three subchronic schizophrenic, and two with paranoid personality disorders) were retested on alternative versions (where available) of the Prorated Verbal IQ, the Wechsler Memory Scale, the California Verbal Learning Test, the Trail Making Test, the Controlled Oral Word Association Test, and the Wisconsin Card Sorting Test 1 week before hospital discharge (on average, 6–8 weeks after they were first tested). All patients demonstrated a substantial reduction in psychotic symptoms as measured by the Scale for the Assessment of Positive Symptoms.

In the statistical evaluation, because the groups differed significantly in age and level of education, a multivariate analysis of covariance (MANCOVA) with age and years of education as covariates was applied to the

scores on the first six summary scales to test for a main effect of group (first-episode patients, patients with chronic schizophrenia, normal subjects). A second MANCOVA was performed on the left hemisphere and right hemisphere scale scores. Scores on the individual neuropsychological tests contributing to the summary scales for which there was an overall effect were subjected to analyses of covariance (ANCOVA) controlled for age and level of education. Post hoc tests were based on Tukey's honestly significant difference for unequal samples (Spjotvoll and Stoline test [21]). These were based on residualized mean square error within cells, adjusted for the covariates. Pearson product-moment correlations were used to test associations between the neuropsychological summary scale scores and scores on the Scale for the Assessment of Negative Symptoms, scores on the Scale for the Assessment of Positive Symptoms, and the duration of illness. Paired t tests were computed for the individual tests of the subgroup of 16 patients, comparing their performances within 2 weeks of admission and within 1 week of discharge. A repeated measures two-group ANCOVA (Group by Hemisphere) was computed to compare the left and right hemisphere scale scores of the two patient groups.

RESULTS

There were statistically significant differences between the three groups, after adjusting for age and education, in scores on the first six summary scales (overall multivariate $F = 2.75$, $df = 12, 146$, $p < 0.002$). The MANCOVA for the left and right hemisphere scale scores was also significant ($F = 6.25$, $df = 4, 154$, $p < 0.0001$). Results on the summary scales are listed in table 2, and results on the individual tests are listed in table 3.

Both the schizophreniform and the chronic patients performed significantly worse than the normal subjects on all of the scales except the language scale, on which only the chronic patients performed worse than the

TABLE 3. Scores on Individual Measures of Neuropsychological Functioning for First-Episode Schizophreniform Patients, Chronic Schizophrenic Patients, and Normal Comparison Subjects

Measure	First-Episode Schizophreniform Patients (N=32) (A)			Chronic Schizophrenic Patients (N=26) (B)			Normal Comparison Subjects (N=25) (C)			ANCOVA	
	Mean	SD	Adjusted Mean	Mean	SD	Adjusted Mean	Mean	SD	Adjusted Mean	F (df=2, 78)	p
Verbal IQ	95.2	16.3	98.1	97.6	14.8	98.8	111.5	17.1	107.4	3.0	0.06
Wide Range Achievement											
Test, Reading subtest	94.5	19.3	96.8	93.2	16.8	96.0	107.8	11.6	102.8	1.6	n.s.
Logical Memory	12.8	6.9	13.5	13.2	7.2	13.5	20.9	5.0	19.8	8.0	0.0007 ^a
Associate Learning	13.4	3.3	13.8	12.9	5.0	13.6	16.9	3.8	15.7	1.6	n.s.
Word Attack	42.9	9.8	43.7	42.9	8.1	43.7	46.9	3.8	45.2	0.7	n.s.
California Verbal Learning											
Test trial 5	9.6	4.1	9.8	9.5	3.7	10.0	13.6	2.3	13.0	6.4	0.003 ^a
Benton Visual Retention Test											
Number correct	6.1	1.8	6.2	5.6	1.9	5.8	8.2	1.6	7.8	9.2	0.0003 ^a
Number of errors	6.0	3.2	5.8	7.2	3.7	6.9	2.9	2.4	3.4	7.6	0.001 ^a
Visual Reproduction	9.5	3.5	9.3	8.5	3.8	9.0	11.8	3.0	11.5	3.8	0.03 ^a
Wisconsin Card Sorting Test											
Number of categories	4.1	2.3	4.2	4.0	2.5	4.3	5.8	0.6	5.5	3.1	0.05 ^b
Number of errors	43.0	25.8	41.9	41.6	31.6	38.2	16.6	10.3	21.0	5.3	0.007 ^a
Number of perseverative responses	29.0	26.3	29.1	31.5	38.3	28.3	9.1	6.5	12.2	3.0	0.06
Booklet Categories Test,											
number of errors	52.1	20.3	50.8	59.4	24.4	57.2	27.1	16.9	30.6	10.5	0.00009 ^a
Stroop Color-Word Test	32.7	10.8	33.0	31.9	11.9	33.3	46.3	12.0	44.6	8.0	0.0007 ^a
Boston Naming Test	50.8	7.0	52.2	51.5	5.2	50.9	54.8	3.7	54.0	2.5	n.s. ^c
Controlled Oral Word Association Test	37.9	9.7	37.7	32.3	9.8	32.3	44.0	9.1	44.2	8.5	0.0004 ^a
Trail Making Test											
A	41.0	18.6	41.1	45.9	30.1	42.4	24.4	14.3	28.0	3.3	0.04 ^c
B	103.3	59.6	99.3	125.7	79.7	113.7	62.3	40.3	78.4	2.3	n.s.
Symbol Digit Modalities Test											
Written	37.6	10.3	37.9	37.7	11.4	39.4	57.2	13.8	55.1	16.5	0.000001 ^a
Oral	43.3	10.7	43.9	42.5	13.2	44.3	65.0	15.8	62.6	16.2	0.000001 ^a
Finger Tapping Test											
Right	46.5	8.3	46.5	42.6	10.6	42.3	51.7	4.3	51.9	7.3	0.001 ^c
Left	42.4	8.5	42.7	40.2	8.1	40.1	46.6	4.7	46.5	4.1	0.02 ^c
Cancellation Test (seconds)	171.1	58.7	166.2	202.6	86.5	196.2	139.4	51.9	150.6	2.9	0.06
Ravens IQ	99.6	14.6	100.8	103.4	16.3	105.3	112.9	9.3	109.7	3.0	0.06
Finger agnosia											
Right	19.3	1.0	19.3	19.3	1.0	19.3	19.7	0.6	19.6	0.9	n.s.
Left	19.4	1.5	19.4	19.3	1.3	19.3	19.6	0.8	19.5	0.1	n.s.
Graphesthesia											
Right	17.1	2.7	17.3	16.8	2.8	16.9	17.8	3.1	17.5	0.3	n.s.
Left	16.3	2.7	16.5	16.7	3.4	17.1	18.4	2.6	17.8	1.4	n.s.

^aSignificant difference between A and C ($p < 0.05$, post hoc Tukey test) and significant difference between B and C ($p < 0.05$, post hoc Tukey test).^bSignificant difference between A and C ($p < 0.05$, post hoc Tukey test).^cSignificant difference between B and C ($p < 0.05$, post hoc Tukey test).

normal subjects, and the sensory/perceptual scale, on which both patient groups performed the same as the normal subjects. Post hoc tests revealed no significant differences between schizophreniform and chronic patients on any neuropsychological summary measure. The repeated measures ANCOVA yielded a main effect for hemisphere ($F=24.5$, $df=1$, 54 , $p < 0.000008$), indicating that left hemisphere function was significantly more impaired than right hemisphere function in both the schizophreniform and the chronic groups. The effect for group and the Group by Hemisphere interaction were not significant in this analysis.

Within the chronic schizophrenic group, separate analyses revealed no differences between patients with the paranoid and nonparanoid (disorganized, undiffer-

entiated) types on any neuropsychological measures. In addition, the MANCOVA and ANCOVAs were recomputed without the data on the four schizoaffective patients in the chronic group. Results identical to those of the original analyses were obtained. Paired t tests (two-tailed) on the 21 test variables indicated that at the second testing, patients performed the same as at the first testing, except for the number of correctly obtained categories on the Wisconsin Card Sorting Test, which was lower ($t=2.1$, $df=15$, $p < 0.05$). Pearson correlations between the neuropsychological summary scale scores and scores on the Scale for the Assessment of Negative Symptoms, scores on the Scale for the Assessment of Positive Symptoms, and the duration of illness yielded no significant associations.

DISCUSSION

Both the schizophreniform and the chronic schizophrenic patients had lower scores on measures of executive function, verbal and spatial memory, concentration/speed, and left and right hemisphere function than the normal comparison subjects. Both patient groups also demonstrated relatively greater left than right hemisphere impairment. These findings indicate that first-episode psychotic patients with the *DSM-III-R* diagnosis of schizophreniform disorder have considerable cognitive dysfunction, comparable to that of chronic patients.

In addition, there was no significant association between length of illness and neuropsychological impairment. Our findings were consistent with other studies of chronic patients showing evidence of global cognitive dysfunction suggestive of both left and right hemisphere involvement (8, 22), but also with other studies which suggest that the left hemisphere may be preferentially affected in schizophrenia (4-7). It should be noted that executive/frontal functions were not significantly more impaired than most other cognitive functions in the patient groups, arguing against the notion of selectivity of frontal lobe involvement in schizophrenia. The patients also demonstrated evidence of verbal and spatial memory deficits, consistent with recent reports of impairment on tasks of temporohippocampal functions (11). Patients appeared to have good sensory/perceptual function.

One possible explanation for the lack of differences between the schizophreniform and chronic schizophrenic groups could have been the effect of acute psychotic state on test results. However, this appeared unlikely, since retest data on the group of 16 patients who were in remission and close to discharge indicated few differences in cognition from that seen at admission. Thus, it appears that the deficits in both groups of patients were not state-related phenomena. In general, there is also little evidence that severity of illness affects neuropsychological test scores (23-25).

Another factor that could have affected the interpretation of the neuropsychological test scores of the schizophrenic patients was medication. In this study, first-episode and chronic patients were taking comparable doses of medication, the only difference being that the chronic patients had been taking medication for approximately 7 years. In general, medication typically improves cognitive performance, particularly on measures of attention and information processing (26). In a recent study by our group (27), patients taking medication performed as well as those not taking medication on almost all neuropsychological measures, with the exception of tests of motor speed.

Our results are consistent with those of longitudinal studies in which cognition was measured before the onset of illness, i.e., during military induction and several years later (12, 13, 28). In general, these studies indicated a decrement in most subtest scores after the onset of illness, thus providing evidence for a fairly rapid decline in cognition associated with the onset of illness.

There is some debate about whether brain morphological changes predate the onset of schizophrenic illness. Ventricular enlargement has been reported in patients close to the onset of illness (29, 30), in patients ill for less than 2 years (31, 32), and in one patient who had not yet developed the illness (33). A number of studies have demonstrated the association of structural abnormalities with neuropsychological deficits (34). Previous studies by our group have shown that some change in brain morphology is evident in the first episode of illness (30). The fact that structural changes have been shown to appear early in illness may explain the degree of cognitive deficit seen in first-episode patients.

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Long-Term Study of the Sleep of Insomnia Patients With Sleep State Misperception and Other Insomnia Patients

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Objective: The objectives were 1) to investigate differences among patients with subjective insomnia (sleep state misperception), patients with objective findings of insomnia, and normal volunteers and 2) to assess the consistency of the sleep findings during a 2-month period. **Method:** Twenty-one subjects were studied. Subjects with sleep state misperception (N=7) had insomnia complaints for more than 1 year, no objective sleep disturbance, and sleep efficiency of 90% or greater (on the diagnostic screening sleep recording), while subjectively estimating that sleep time was less than 6.5 hours. Subjects with objective insomnia (N=7) met the same subjective criteria, but objectively sleep efficiency was 85% or less. Normal subjects (N=7) had no insomnia complaints and objective sleep efficiency of 90% or greater. All subjects were recorded on 2 consecutive nights three times with a 3-week period between each pair of nights (6 standard all-night polysomnographic sessions of 8 hours). A subjective sleep questionnaire was administered after each sleep recording night. **Results:** Sleep stage variables (percentages) were similar between the two insomnia groups, and both were different from the normal subjects. Sleep continuity variables were disturbed in the objective insomnia group, but they were similar in the sleep state misperception and normal groups. Both insomnia groups rated their sleep as inadequate on the questionnaires and differed from the normal subjects. The distinct sleep patterns of each of the three groups did not vary over the 6 nights of assessment. **Conclusions:** Sleep state misperception may be a prodromic or transitional state of sleep dysfunction between normal sleep and the sleep pattern of objective insomnia.
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Insomnia with no objective findings in the first (1979) Diagnostic Classification of Sleep and Arousal Disorders (1), or sleep state misperception in the 1990 International Classification of Sleep Disorders (2), is a disorder in which there is a complaint of insomnia but no polysomnographic evidence of a sleep disturbance. Objective sleep disturbances have been reported in all other insomnia diagnostic categories. These sleep disturbances have typically included a longer sleep latency and shorter sleep continuity (3). In addition, sleep stage alterations have been reported in objective insomnia but not in sleep state misperception. The amount of slow-wave sleep is less and the amount of stage 1 is greater in objective insomnia patients than in age- and sex-matched control subjects

(4, 5). The amount of REM sleep has not been found to be different.

Previous studies (6, 7) reporting that the sleep of patients with sleep state misperception does not differ from that of normal subjects typically used 1 to 3 nights of polysomnographic recording. However, it has been reported that patients with insomnia have high night-to-night variability in the quality of their sleep (8). This variability is particularly apparent during placebo conditions in longitudinal psychopharmacological studies of such patients (9). Previous studies have shown that insomnia patients have disturbed sleep on approximately 50% of the nights. Hence, on the basis of probability theory, a 5-night sample would be required for identifying, with greater than 95% confidence, sleep disturbance in patients with sleep state misperception insomnia. Thus, it has been argued that sleep state misperception is a pseudodiagnostic category (10) in that the diagnosis is typically made on the basis of an inadequate sample of sleep (i.e., 1 to 3 nights).

Another issue in evaluating the validity of sleep state misperception was raised in a recent review (11). The review questioned the need for a subclassification of the

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DSM-III-R diagnosis of primary insomnia under which the sleep state misperception diagnosis of the International Classification of Sleep Disorders would fall. It was argued that sleep state misperception is a characteristic of all chronic insomnias and that such patients are merely at one extreme of a continuum. However, the review clearly indicated that factors which determine how sleep is subjectively assessed are not known. Given an adequate sample of the sleep of patients who misperceive their sleep, information regarding the presence or absence of consistent sleep stage differences in such patients compared to other insomnia patients and normal subjects will provide a basis for further evaluating the validity of sleep state misperception.

The first objective of the present study was to evaluate the consistency of sleep in sleep state misperception insomnia. This was done during a 2-month period with 2-night samples every 4 weeks. Given a larger sample of the sleep of patients with sleep state misperception, a second objective was to compare the polysomnographic characteristics of such patients to those of patients with insomnia with objective findings and age-matched normal subjects. These data were collected as the baseline nights before each of three conditions in a larger study of the self-administration of benzodiazepine hypnotics.

METHOD

Subjects

Twenty-one men and women (seven subjects per group) 30–50 years of age were studied. All were in good health (except for a complaint of insomnia) as determined by the screening procedure. All the subjects were recruited through a newspaper advertisement stating: "Wanted: healthy men & women, with or without difficulty sleeping, 18–55 years of age, for participation in sleep studies." All subjects gave written informed consent and received payment for their participation.

Procedure

Subjects underwent a medical history, a physical examination, and laboratory blood and urine tests before a screening nocturnal polysomnogram. Subjects were excluded if they had acute or chronic medical conditions that required treatment or were currently taking CNS-active drugs. Urine drug screening was used to verify subjects' reports. Anyone with a history of psychiatric disorders, drug addiction, or alcoholism was excluded. Finally, anyone who had taken a benzodiazepine hypnotic within the past year was also excluded.

Each subject underwent a sleep disorders evaluation including a sleep history and a nocturnal polysomnogram. Evaluations also included a psychometric battery consisting of the MMPI and the Profile of Mood States (POMS). Subjects recruited as normal subjects reported no history of insomnia, estimated their nightly

sleep time as greater than 7 hours, and had a sleep efficiency on the screening nocturnal polysomnogram of 90% or greater. There were four women and three men in this group; the mean age was 35.6 years ($SD=5.9$). Subjects qualifying as patients with sleep state misperception insomnia had more than a 1-year history of insomnia, estimated their nightly sleep time as less than 6.5 hours, had a sleep efficiency of 90% or more on the diagnostic polysomnogram, and underestimated their sleep time for the diagnostic night by at least 1 hour. There were three women and four men in this group; the mean age was 36.4 years ($SD=5.9$). Insomnia subjects with objective findings were included in the study if they had more than a 1-year history of insomnia, estimated their nightly sleep time as less than 6.5 hours, and had a sleep efficiency of 85% or less. There were four women and three men in this group; the mean age was 35.4 years ($SD=6.3$). All subjects had no evidence of apnea or periodic leg movements on the nocturnal polysomnogram.

Those subjects who passed the diagnostic screening were entered into the study within 1 week of having qualified. On study nights subjects arrived at the sleep laboratory 1.5 hours before their usual bedtime, which was held constant throughout the study. They were prepared for standard polysomnographic assessment. A standard all-night polysomnogram was obtained on each of the 6 nights. A set of 2 nights was recorded three times, with an interval of 4 weeks between samples.

The polysomnogram included the central and occipital EEG, electro-oculogram, and submental electromyogram (EMG) collected from standard placements and monitored continuously for 8 hours. The diagnostic screening also included nasal and oral respiration measured with thermistors and bilateral leg (anterior tibialis) EMG. Subjects were awakened after 8 hours in bed. After arising each morning they completed a sleep questionnaire regarding the quantity and quality of the previous night of sleep.

The following study restrictions were adhered to by all participants: 1) no alcoholic or caffeinated beverages after 4:00 p.m. on study nights, 2) no napping during the study, 3) no changes in bedtimes or wake times during the study, 4) 8 hours in bed each night during the study, and 5) no medication without approval of the investigator.

Each polysomnographic recording was scored manually in 30-second epochs according to the standards of Rechtschaffen and Kales (12). Records were coded so that scorers were unaware of the participants' group. Variables reflecting sleep continuity included total sleep time, defined as number of nonwake epochs from the beginning of the recording to the end divided by two; wake time during sleep, the number of wake epochs (divided by two) after the onset of persistent sleep (10 minutes of continuous sleep) before final awakening; latency to persistent sleep, the number of epochs from beginning of recording to the start of the first 20 epochs of nonwake divided by two (i.e., 10 minutes of continuous sleep); and number of awakenings, the number of

TABLE 1. Objective Sleep Continuity Variables in Patients With Sleep State Misperception or Objective Insomnia and in Normal Subjects

Sleep Variable	Night												Significant Post Hoc Group Comparisons (p<0.05)
	1		2		3		4		5		6		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Total sleep time (min) ^a													C=A, B<C, B<A
Sleep state misperception (A)	454.0	28.7	457.5	25.6	453.1	17.3	463.3	12.1	453.7	28.7	453.8	17.6	
Insomnia(B)	426.8	40.1	438.1	24.2	383.3	83.0	407.4	45.6	422.3	30.5	433.7	35.3	
Normal (C)	441.7	43.0	454.4	15.9	465.2	13.1	459.5	23.5	450.4	13.1	439.8	25.8	
Latency to persistent sleep (min) ^b													C=A, B>C, B>A
Sleep state misperception (A)	10.7	11.2	8.8	6.7	18.2	11.8	11.4	17.4	20.0	27.9	12.7	11.6	
Insomnia (B)	24.1	39.6	23.3	22.1	20.2	13.8	28.0	27.3	35.6	26.1	13.7	11.4	
Normal (C)	18.8	19.1	16.2	14.3	6.8	6.5	9.5	10.6	9.9	9.6	12.7	16.0	
Wake during sleep (min) ^c													C=A, B>C, B>A
Sleep state misperception (A)	15.1	19.1	8.7	8.9	10.7	10.1	10.7	8.4	9.4	11.4	10.1	8.4	
Insomnia (B)	36.1	27.7	19.6	14.8	43.2	49.8	45.2	40.8	24.0	26.7	31.7	39.7	
Normal (C)	17.2	25.4	9.7	9.1	9.1	10.4	12.4	17.2	19.5	10.8	25.6	26.1	
Number of awakenings ^d													C=A, B>C, B>A
Sleep state misperception (A)	4.4	2.9	2.5	1.7	3.3	2.3	4.1	3.7	3.4	3.5	4.5	3.4	
Insomnia (B)	8.1	5.5	6.4	4.9	4.0	3.3	4.7	3.9	8.5	8.8	8.0	11.5	
Normal (C)	3.1	3.3	4.0	3.5	2.8	3.1	4.7	6.5	4.0	3.6	6.7	6.6	

^aSignificant group effect (F=15.7, df=2, 18, p<0.00001).^bSignificant group effect (F=4.92, df=2, 18, p<0.009).^cSignificant group effect (F=10.33, df=2, 18, p<0.0002).^dSignificant group effect (F=3.81, df=2, 18, p<0.02).**TABLE 2. Subjective Sleep Continuity Variables in Patients With Sleep State Misperception or Objective Insomnia and in Normal Subjects**

Sleep Variable	Night												Significant Post Hoc Group Comparisons (p<0.05)
	1		2		3		4		5		6		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Total sleep time (min) ^a													C>A, C>B, A=B
Sleep state misperception (A)	395.7	26.5	377.1	57.8	347.8	76.1	365.0	51.2	381.8	58.8	397.1	60.6	
Insomnia (B)	333.5	108.8	387.8	74.2	337.8	126.2	289.3	143.0	365.7	125.4	352.8	129.2	
Normal (C)	456.4	43.2	460.0	26.3	466.7	12.6	469.3	9.7	447.1	39.9	470.0	11.5	
Latency to persistent sleep (min) ^b													C<A, C<B, A=B
Sleep state misperception (A)	33.5	16.2	50.7	31.3	47.1	16.7	42.1	38.1	42.5	38.4	47.1	31.7	
Insomnia (B)	39.3	30.4	25.3	10.6	38.9	17.3	48.9	36.3	37.5	36.6	37.8	35.8	
Normal (C)	16.4	20.4	19.2	13.3	8.7	4.6	8.5	4.8	12.3	8.2	10.2	7.7	
Wake during sleep (min) ^c													C<A, C<B, A=B
Sleep state misperception (A)	37.8	26.4	50.1	47.5	67.1	62.5	67.1	37.0	55.5	42.2	33.6	28.3	
Insomnia (B)	73.6	63.5	29.3	41.7	78.5	110.9	80.1	105.6	60.7	97.4	66.8	79.7	
Normal (C)	15.3	20.8	7.1	9.4	6.1	6.1	5.8	5.9	25.0	42.1	14.8	20.4	

^aSignificant group effect (F=24.3, df=2, 90, p<0.00001).^bSignificant group effect (F=17.81, df=2, 18, p<0.00001).^cSignificant group effect (F=9.46, df=2, 18, p<0.0004).

entries to wake from persistent sleep that were of at least two consecutive epochs' duration. Variables reflecting sleep architecture included percentage of time in each sleep stage, which was obtained by dividing minutes of the stage by total sleep time multiplied by 100; and the latency to REM sleep, the number of non-wake epochs from beginning of recording to the first epoch of stage REM divided by two.

Mixed-design analyses of variance (SAS) (13) were conducted on the various polysomnographic measures, with group as the between-subjects factor and night as the within-subjects factor. Conservative probability levels, corrected by the Greenhouse-Geisser procedure, were used for all within-subjects comparisons.

RESULTS

Variables reflecting the efficiency of sleep are shown in table 1. Total sleep time was similar in the normal and sleep state misperception groups, while the objective insomnia group differed from the other two groups. There also was a group effect in the latency to persistent sleep, wake during sleep, and number of awakenings. The objective insomnia group was the main source of statistical differences compared to the two other groups. The normal and sleep state misperception groups were similar, which is consistent with the diagnostic screening night. With regard to the first objective of the study, there was no night effect or

TABLE 3. Sleep Architecture Variables in Patients With Sleep State Misperception or Objective Insomnia and in Normal Subjects

Sleep Stage	Mean	SD	Significant Post Hoc Group Comparisons (p<0.05)
Total sleep time (min) ^a			C=A, B<C, B<A
Sleep state misperception (A)	455.9	21.4	
Insomnia (B)	418.0	8.1	
Normal (C)	451.8	24.9	
Percent of stage 1 ^b			B=A, A>C, B>C
Sleep state misperception (A)	14.0	4.4	
Insomnia (B)	14.4	9.9	
Normal (C)	11.2	3.1	
Percent of stage 2 ^c			C<A, C<B, A<B
Sleep state misperception (A)	55.1	6.4	
Insomnia (B)	59.5	12.4	
Normal (C)	51.9	6.1	
Percent of stages 3-4 ^d			C>A, C>B, B<A
Sleep state misperception (A)	11.9	6.2	
Insomnia (B)	7.0	5.5	
Normal (C)	14.7	7.2	
Percent REM stage ^e			B=A, A<C, B<C
Sleep state misperception (A)	18.9	5.6	
Insomnia (B)	18.9	5.6	
Normal (C)	22.5	6.4	
REM latency (min)			
Sleep state misperception (A)	77.6	38.1	
Insomnia (B)	83.4	38.8	
Normal (C)	79.5	37.3	

^aSignificant group effect (F=15.7, df=2, 18, p<0.001).

^bSignificant group effect (F=3.61, df=2, 18, p<0.06).

^cSignificant group effect (F=7.55, df=2, 18, p<0.001).

^dSignificant group effect (F=15.23, df=2, 18, p<0.001).

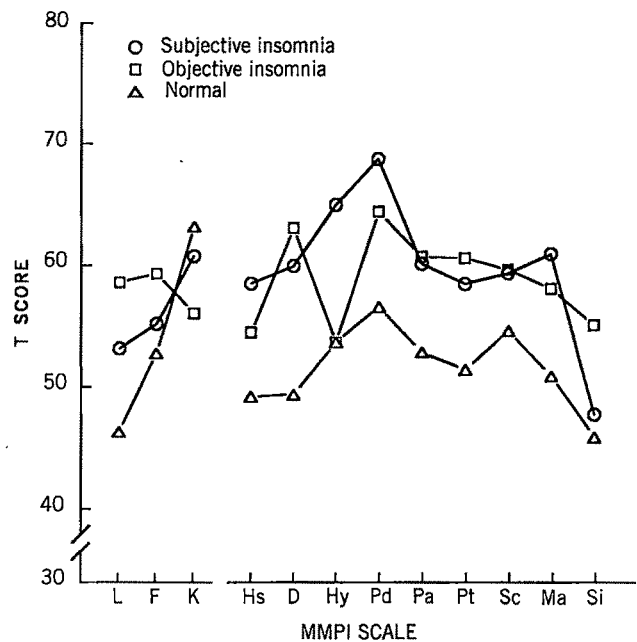
^eSignificant group effect (F=5.57, df=2, 18, p<0.05).

Group by Night interaction, which suggests relatively consistent findings over the 6 nights.

Table 2 displays the subjective assessment of sleep obtained on the questionnaires on the 6 nights for each group. Differences between the groups were found on each variable. The two groups with insomnia complaints were similar and differed from the age- and sex-matched normal subjects in estimated total sleep time, wake during sleep, and latency to sleep. Again, relative to objective 1 of the study, there was no night effect or Group by Night interaction.

Sleep architecture is shown in table 3. A 6-night average of each group is presented. Percentage of stage 1 was similar in the two insomnia groups, and they were higher than the normal group. Percentage of stage 2 was different among the three groups. Delta sleep percentage (sleep stages 3-4) was lower in both insomnia groups and was lowest in the objective insomnia group. Percentage of REM sleep was not different between the objective and sleep stage misperception groups, but both groups had less REM sleep than the normal group. REM sleep latency did not differ among the three groups.

The MMPI profiles of the three groups are illustrated in figure 1. The objective insomnia subjects showed the typical MMPI pattern previously reported for such patients, significantly higher scores on the hypochondriasis (Hs) and depression (D) scales than the normal sub-

FIGURE 1. MMPI T Scores of Patients With Sleep State Misperception (Subjective) Insomnia (N=7) and Objective Insomnia (N=7) and Normal Subjects (N=7)^a

^aThe objective insomnia patients had significantly higher scores on the hypochondriasis and depression scales than the normal subjects (F=3.48, df=2, 18, p<0.03; F=4.59, df=2, 18, p<0.02). The subjective insomnia patients had significantly higher hysteria scale scores than the normal subjects (F=8.43, df=2, 18, p<0.01).

jects. The subjective insomnia subjects were similar to the objective insomnia subjects and also had significantly higher hysteria (Hy) scale scores than the normal subjects. As illustrated, the T scores of both insomnia groups, while different from those of the normal subjects, were not pathologically elevated (i.e., T score more than 70). No group differences in POMS scores were observed.

DISCUSSION

The results of this study showed that the sleep of patients with sleep state misperception was relatively consistent over a 2-month period comparable to normal subjects and other insomnia patients. None of the analyses showed a night effect or an interaction of nights with groups. That is, patients with sleep state misperception consistently showed sleep efficiencies similar to those of the healthy normal subjects, while subjectively experiencing disturbed sleep like that of the other insomnia patients.

The second goal of the study was to determine if group differences in sleep might be detected when a larger sample of sleep was obtained. The major finding with respect to this question was that sleep stage variables were similar in the two insomnia groups but different from the normal group, while variables reflecting

sleep induction and continuity were disrupted only in the objective insomnia group and were similar in the normal and sleep state misperception groups. That is, the larger sample of sleep did reveal differences in sleep staging between sleep state misperception patients and healthy normal subjects.

One important interpretive caution in this study is that the insomnia patients were recruited through the newspaper. Stepanski et al. (14) found no differences in sleep measures between a group of insomnia patients referred by their physicians and a second group of self-referred insomnia patients recruited through the newspaper. However, significant differences were found on psychometric measures and measures of daytime alertness. For this reason, the way in which the patients in the present study were recruited may be a limitation of the study.

Given that precaution, the higher percentages of stages 1 and 2 sleep and lower percentage of stages 3–4 sleep in the sleep state misperception group may explain the disparity between the objective (i.e., polysomnographic) and subjective (i.e., questionnaire) evaluation of sleep. The sleep state misperception group rated their sleep as inadequate on the postsleep questionnaires. It is possible that the lesser amount of deep sleep (i.e., stages 3–4) and greater amount of light sleep (i.e., stage 1) account for sleep misperception in this group. The objective insomnia group also had a misperception of the amount of sleep, albeit less than that of the sleep misperception group.

These data are consistent with the suggestion of Reynolds et al. (11) that sleep state misperception is a characteristic of all insomnia patients. However, these data do suggest that there is a group of patients who complain of poor sleep but have "normal" sleep induction and sleep continuity. Although misperception of sleep is a characteristic of all patients with insomnia, this group represents the extreme of the continuum.

The polysomnographic findings of normal sleep continuity, but sleep stage differences, suggests that sleep state misperception may be a transitional state between normal sleep and a more extreme insomnia condition. In this view, in some insomnia patients, or in the early stages of all insomnia, sleep homeostatic processes produce a redistribution of sleep stages (i.e., more time spent in stages 1 and 2 and less in stages 3–4). In the latter stages of insomnia or in more severe insomnia, sleep homeostatic processes fail and frank wakefulness is observed. Thus, sleep state misperception might be considered the prodromic stage of a future psychophysiological insomnia.

On the other hand, one could argue that sleep state misperception is a distinct subclassification of primary

insomnia. The difference between patients with sleep state misperception and other insomnia patients in MMPI profile, particularly on the hysteria scale, supports such a view. This might suggest that there is a vulnerable personality characteristic that predisposes an individual to development of sleep state misperception.

Finally, whether the subclassification of sleep state misperception has validity and clinical utility hinges on whether it has a distinct etiology, course, and treatment response. At this time there is insufficient information to reach any conclusions. More prospective studies of these patients over time and assessment of their treatment response are needed before any conclusions can be reached.

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Conservatorship for Gravely Disabled Psychiatric Patients: A Four-Year Follow-Up Study

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Objective: The authors examined the conservatorship process in California by studying a group of psychiatric patients for whom conservatorship was sought; their goal was to determine its effectiveness both during and after the period of conservatorship. **Method:** The subjects were 60 county psychiatric hospital inpatients 18–60 years old for whom temporary (30-day) conservatorships were obtained and who were followed for 4 years. The patients' courses over the 4 years were assessed in terms of whether 1-year conservatorships were obtained, stability (number and length of psychiatric hospitalizations, arrests, serious physical violence, and homelessness), and presence or absence of family support. **Results:** The patients proved to be a severely mentally ill and disabled group. Thirty-five (58%) were granted a 1-year conservatorship sometime during the 4-year study period, and 25 (42%) were not. Both family support and conservatorship appeared to be related to the patients' stability. When one or both were present, there was a significantly greater likelihood of stability. **Conclusions:** The authors believe that for a considerable number of chronically and severely mentally ill individuals, conservatorship would play an important role in their clinical management and treatment by helping to eliminate their chaotic life styles, their cycle of admission and discharge from hospitals and jails, and/or their living on the streets, particularly when family support is absent.

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The provisions for conservatorship of mentally ill individuals in California's Lanterman-Petris-Short Act of 1968 were intended to "allow another individual or agency to act on the person's behalf and to protect his interests when he is unable to care for himself. The conservator may determine what arrangements are necessary to provide the conservatee with food, clothing, shelter, and further treatment, and he may take any appropriate steps necessary to safeguard the person's property" (1, p. 23).

Conservatorship has been supported by many as enabling individuals who would otherwise be long-term residents of psychiatric hospitals to live in the community and achieve a considerable measure of autonomy in their lives (2–4). The argument has been made that by giving up some of their liberty, many conservatees, who would otherwise need to be hospitalized for long periods of time, are able to retain most of their independence and their community status.

Conservatorship based on grave disability has been criticized by a few as having essentially retained long-term commitment and as having imposed involuntary

treatment for the nondangerous mentally ill, conditions they hoped would be eliminated by the new involuntary commitment laws (5–7). These critics, however, do not oppose involuntary treatment for the dangerous mentally ill. They voice concern that conservatorship is a way of maintaining a need for treatment standard and achieving social control over individuals who do not meet the strict criterion of danger to self or others.

The purpose of this article was to study the conservatorship process for individuals 18–60 years old, to describe a group of patients for whom conservatorship was sought, and to ascertain its effectiveness both during and after the period of conservatorship. Does conservatorship enhance community tenure? Does it promote stability of the patient's mental condition and life situation? To what extent does family support and involvement affect and interact with the conservatorship process?

THE CONSERVATORSHIP PROCESS IN CALIFORNIA

Conservatorship proceedings are sought for individuals considered gravely disabled, which, in California, means "a condition in which a person, as a result of a mental disorder, or impairment by chronic alcoholism, is unable to provide for his or her basic personal needs for food, clothing or shelter" (8). Many have accepted the case law interpretation (9–11) that a person is not

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"gravely disabled" if he or she is capable of surviving safely in freedom with the help of willing and responsible family members, friends, or third parties. However, if an individual is gravely disabled and is unwilling or unable to accept treatment voluntarily, a conservatorship may be recommended. Most of these recommendations are made after a relatively short period of involuntary hospitalization (i.e., 17 days); however, there are conditions under which a person may be recommended for conservatorship who has not been in an inpatient facility.

Recommendations for conservatorship may be made only by professionals in charge of agencies providing comprehensive evaluation and/or intensive treatment. Generally, the proceedings begin with a period of temporary conservatorship that usually does not exceed 30 days. At this time, the court schedules a conservatorship hearing to follow the expiration of the temporary conservatorship period and appoints a temporary conservator from the public guardian's office or a similar agency. The temporary conservator's role is to determine and arrange for the patient's food, shelter, and care while awaiting the conservatorship hearing. During this period, an evaluation and investigation are also conducted to determine if alternatives to conservatorship are available and to assess the needs of the patient. Irrespective of whether a conservatorship is recommended after the temporary conservatorship has been obtained, the case is reviewed by the court. Moreover, if a conservatorship is recommended, the patient has a right to a court or jury trial.

If the court or jury accepts the recommendation, the patient is placed under a conservatorship for 1 year, which can be renewed at the end of the 1-year period. The conservatorship can also be terminated before the 1-year period is over. Conservatees are entitled to judicial reviews of their status every 6 months.

The court appoints a conservator who is either a private individual or a public agency, e.g., the public guardian's office. The conservator may be granted a number of powers over the conservatee, including those of estate. However, the most commonly granted powers are those related to the conservatee's residential placement, involvement in psychiatric treatment, and management of the conservatee's money. That is, the conservator has the power to place the conservatee anywhere (e.g., at home, in a board and care facility, in a locked skilled nursing facility, or in a psychiatric hospital) and to require that the conservatee attend psychiatric treatment and take medications to remedy or prevent "the recurrence of the conservatee's being gravely disabled" (12).

METHOD

The study subjects consisted of all individuals 18–60 years old in the Los Angeles County/University of Southern California (USC) Psychiatric Hospital for whom temporary (30-day) conservatorships were obtained from January 1, 1986, through March 15, 1986.

This time period was chosen to allow for a 4-year follow-up period in 1990. During the 1986 time period, temporary conservatorships were obtained for 71 individuals. In five cases, both the patient and the family spoke only Spanish and therefore were not included in the study. Three patients were transients who were returned to their home states before the conservatorship proceedings could be concluded; these were also dropped from the study. Of the remaining 63 patients, there was insufficient information for three patients to provide an adequate 4-year follow-up. Thus, the 4-year follow-up group numbered 60.

This study was conducted under the auspices of both the Los Angeles County Superior Court (all conservatorship hearings in the county are held in this court) and the Los Angeles County/USC Psychiatric Hospital, the largest hospital in the county. Both court and hospital records were reviewed, as well as records in the Los Angeles County Department of Mental Health Computerized Management Information System. In some cases, the patient's course over the 4 years and status at 4-year follow-up could be obtained entirely from court and psychiatric records. For the remaining cases, we obtained this information from family and/or friends, staff of board and care homes and other residential facilities in which the patient had been placed, and mental health professionals involved with the patient.

Instability during the 4-year follow-up period was defined as placement in the community marked by 1) a total of 6 months or more of psychiatric hospitalization or 2) a total of 3 months or more of psychiatric hospitalization plus one or more of the following: serious physical violence against others, arrests involving time in jail, and homelessness. Family support was defined as strong, consistent involvement and willingness to provide assistance in the form of living arrangements, emotional support, structure, management of finances, and monitoring of medications, nutrition, and health.

RESULTS

The 60 patients ranged in age from 18 to 60 years (median=35 years). Twenty-nine (48%) were men and 31 (52%) were women. Their educational levels ranged from the fifth grade to 1 year of graduate school (median=4 years of high school). Other characteristics of the 4-year follow-up group are given in table 1.

All 60 patients were placed on a temporary conservatorship during the index admission. Of these, 35 (58%) were granted a 1-year conservatorship sometime during the 4-year study period and 25 (42%) were never granted a 1-year conservatorship during the 4-year period. These two groups did not differ significantly on any of the demographic data given in table 1.

Family Support and Stability

The 60 patients were not randomly placed in the conservatorship and nonconservatorship groups. Rather,

TABLE 1. Characteristics of 60 Patients for Whom Temporary (30-Day) Conservatorships Were Obtained

Characteristic	Number	Percent
Race		
White	24	40
Black	23	38
Hispanic	10	17
Asian	3	5
Marital status		
Never been married	37	62
Married	3	5
Divorced or separated	17	28
Widowed	3	5
Primary diagnosis (<i>DSM-III-R</i>)		
Schizophrenic disorders	27	45
Schizoaffective disorders	8	13
Major affective disorders	23	38
Organic mental disorders	2	3
History of serious substance abuse	34	57
Living situation at time of index hospitalization		
With family	23	38
Own apartment or home	11	18
Board and care home	6	10
Hotel	2	3
Mission	1	2
On the streets	16	27
Unknown	1	2
Source of support		
Employment	5	8
Family	7	12
Supplemental Security Income or Social Security Disability Insurance	39	65
Worker's Compensation	1	2
County general relief	1	2
Aid to Families With Dependent Children	1	2
No known source of support	6	10
History of psychiatric hospitalization ^a	57	95
State hospital	31	52
Forensic mental hospital	5	8
County, private, or Veterans Administration hospital or psychiatric ward of general hospital	54	90
History of outpatient treatment	40	67
Previous arrest	20	33
History of physical violence against persons	30	50
History of residence in a board and care home	18	30
Held at least one job 6 months or longer	24	40

^aTypes of hospitalizations add up to more than 57 because all previous hospitalizations were counted.

they fell into these two groups for a variety of reasons: clinical judgment on the part of the treatment staff based on the patient's clinical course; past history and available resources after discharge, including alternatives to conservatorship; the judgment of the court on these matters; and the wishes of the patient's family. Nevertheless, comparison of the group of patients placed on conservatorship and the group of patients not placed on conservatorship reveals a striking finding with respect to family support and the patient's stability during the 4-year study period (table 2). For those patients who were placed on conservatorship, there was no significant difference in their stability or instability

TABLE 2. Family Support and Stability During 4-Year Follow-Up of 60 Patients for Whom Temporary (30-Day) Conservatorships Were Obtained

Support Measure	Patients Placed on 1-Year Conservatorship (N=35)		Patients Not Placed on 1-Year Conservatorship (N=25)	
	Stable	Unstable	Stable	Unstable
Family support	12	6	11	3
Absence of family support	8	9	0	11
Total	20	15	11	14

and whether or not they had family support from the time of their conservatorship to the end of the 4-year study period ($\chi^2=1.37$, $df=1$, *n.s.*). However, for those patients who were never placed on conservatorship during the 4-year study period, there was a highly significant relationship between their stability or instability and the presence of family support ($\chi^2=12.41$, $df=1$, $p<0.001$, Yates' correction).

Of the 29 patients who had unstable courses, all had hospitalizations of 3 months or more, 15 (52%) had hospitalizations totaling 6 months or more, 14 (48%) had been arrested, 16 (55%) had been physically violent against persons, and 11 (38%) had been homeless. There were no significant differences in these areas between those placed on conservatorship and those not. All 29 patients had on numerous occasions showed signs of decompensation that were not promptly and consistently addressed.

Conservatorship and Stability

Of the 35 patients who were placed on conservatorship, 29 (83%) remained stable as long as the conservatorship lasted. However, 21 (60%) of the 35 patients had their conservatorship terminated during the 4-year study period. Of these 21 patients, only nine (43%) remained stable after termination. Of the 12 remaining patients who became unstable, eight manifested instability within 6 months of termination of conservatorship.

Of the total group of 35 patients placed on conservatorship, the mean length of time actually on conservatorship was 26.7 months (median=24 months). While actually on conservatorship, the mean total length of time psychiatrically hospitalized was 14.1 months, or 53% of the time on conservatorship (median percentage=50%).

DISCUSSION

This was a 4-year follow-up study of patients in a county psychiatric hospital for whom temporary conservatorships were obtained under California's Lanterman-Petris-Short Act. The typical patient in this study had a schizophrenic or major affective disorder and a

history of multiple psychiatric hospitalizations and outpatient psychiatric treatment. Almost three-fifths were known to have a history of serious substance abuse, half were known to have a history of physical violence against persons, and one-third were known to have previous arrests. Over one-fourth of the patients were living on the streets at the time of the index hospitalization. These findings are not surprising in a group of psychiatric patients classified as gravely disabled.

Follow-up of the study group revealed two subgroups: 35 (58%) patients who were granted a conservatorship sometime during the 4-year study period and 25 (42%) who were never granted a conservatorship. These two groups differed in the relationship between their stability and their family support. For those patients who were never placed on conservatorship, there was a highly significant relationship between the presence of family support and stability. This is in marked contrast to the group who were placed on conservatorship, where there was no significant relationship between family support and stability. These results suggest that the presence of family support may well obviate the need for conservatorship in a number of individuals who would otherwise need it. On the other hand, if the patient improves in the hospital and family support is absent, clinicians should more carefully consider pursuing conservatorship rather than simply dropping the process.

Family Support

Family support in this study often took the form of patients living with families who provided considerable emotional support, monitored the patients' medications and all other aspects of their treatment and rehabilitation, and supervised the patients' money. In other cases, the family convinced the patients that they should live in a supervised setting such as a board and care home but remained involved with the patient by means of frequent visits, working with the board and care home operator on issues of daily living and management of the patient's money. In still other cases, patients lived in a nearby apartment but took their meals with the family and spent considerable time with them.

Looking at the patients who were actually placed on conservatorship, we found further important results. Twenty-nine (83%) of the 35 patients placed on conservatorship remained stable as long as the conservatorship lasted; for the 21 patients whose conservatorship was terminated, only nine (43%) remained stable after termination. Thus, remaining on conservatorship may be a factor contributing to stability. Two-thirds of those who became unstable did so within 6 months of termination of conservatorship.

While the patients were actually on conservatorship they spent an average of approximately half of the time in psychiatric hospitals. For some, conservatorship became a mechanism for long-term involuntary hospitalization. For others, conservatorship permitted intermediate periods of hospitalization in order to achieve

stabilization. For still others, conservatorship appeared to be a key factor in helping to maintain chronically and severely mentally ill individuals in the community.

A case example will illustrate some of the points made here. Minor changes have been made in some of the facts of the case to preserve confidentiality.

Case Example

This 40-year-old divorced woman had her first episode of schizophrenia, paranoid type (*DSM-III-R*), when she was 19 years old, resulting in hospitalization. Over the years she had a number of rehospitalizations. Her marriage of less than a year ended in divorce when she was 28 years old. For 10 years, she lived in numerous board and care homes in her home state. Each time, as she began to feel emotionally close to the board and care staff and residents, she would become increasingly anxious and paranoid and go to live in another board and care home. Finally, she came to California "to better her life." However, for the 2 years before the index hospitalization, she had been living on the streets of Los Angeles. Bizarre behavior brought her to the attention of the police, who transported her to the county psychiatric hospital. In the hospital, she had a stormy course and would agree to no reasonable discharge plans. She had no family support in the area. A conservatorship was obtained, and the public guardian's office was named conservator. After 2 months in the county hospital, the patient was transferred to the state hospital, where she remained for 10 months. The conservatorship was renewed and the patient was discharged to the community. She lived in a board and care home and attended outpatient treatment for several months, when her family in her home state petitioned the court to allow the patient to return to her home state. The patient had not been willing to do this but now she readily agreed. The conservatorship was terminated and the patient went to live with a sister on a temporary basis. After a few months, the patient entered a satellite housing program but maintained a close relationship with her sister, who was extremely supportive. A year later, the sister was transferred to another state, and several weeks after the move the patient, now without her support and involvement, decompensated. At the 4-year follow-up date, the patient was in the state hospital where she had been since her sister's departure. The sister was concerned but expressed helplessness with regard to her ability to help the patient from afar.

Conservatorship enabled this patient to become stabilized during a hospitalization of approximately 1 year. She was then willing, as she had not been before, to accept the support and structure offered by her family. The importance of this is shown by her stability when she had strong family support and her prolonged decompensation immediately after this support was withdrawn. Thus, this patient was stable while on conservatorship or while she had family support but unstable when she had neither.

CONCLUSIONS

The subjects of this study were patients for whom temporary conservatorships were obtained. These patients proved to be severely mentally ill and disabled.

They fell into two groups: those who were granted a conservatorship sometime during the 4-year study period (58%) and those who were not (42%). Both family support and conservatorship appeared to be related to stability. When one or both were present, there was a significantly greater likelihood of stability in terms of absence of problem areas, such as number and length of psychiatric hospitalizations, arrests, physical violence, and homelessness. When both family support and conservatorship were not present, stability was significantly less likely.

Conservatorship based on grave disability frequently embodies a need for treatment standards for nondangerous patients. We believe this is a more humane approach than the alternative of simply doing nothing for patients too ill to accept treatment. In particular, when family support is not available, conservatorship can mean the difference between a life style characterized by chaos and a life that includes the opportunity to be free from the dysphoria resulting from being admitted to and discharged from hospitals and jails and/or on the streets.

For a considerable number of chronically and severely mentally ill individuals, conservatorship would play an important role in their clinical management and treatment. Conservatorship does not necessarily eliminate intermediate or long-term psychiatric hospitalization; in a number of cases it facilitates it. However, in

many cases, by giving up a little of their liberty through the conservatorship process, these individuals are able to avoid long-term hospitalization and thus retain most of their freedom.

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Differences in the Effects of Divorce on Major Depression in Men and Women

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***Objective:** The authors examined the relationship between marital disruption and major depressive episodes. **Method:** The analyses were based on longitudinal, community-based data from the New Haven Epidemiologic Catchment Area (ECA) program on respondents 18–60 years old. The presence and history of major depression was assessed by using the National Institute of Mental Health Diagnostic Interview Schedule. **Results:** Marital disruption was associated with higher prevalence rates of major depression in both men and women, but only men had a greater risk of a first-onset major depression. Differences between men and women in rates of major depression were observed only among married subjects. **Conclusions:** These findings suggest that the relationship between marital disruption and major depressive episode differs for men and women. They also provide further evidence that differences between men and women in rates of depression vary by marital status.*

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In the United States, marriages have a substantial likelihood of ending in divorce (1, 2). Although there is little doubt that marital disruption is associated with considerable emotional turmoil (3), the extent to which marital separation or divorce is a risk factor for a major depressive episode is unclear. Most information on the relationship between marital status and clinical assessments of depression has been drawn from cross-sectional community studies (4, 5) or studies of psychiatric patients (6, 7). In both types of studies, a history of depression before the changes in marital status is not assessed, so that groups at risk for first-onset episodes are determined by potentially biased retrospective reports. The only available longitudinal data in community samples come from studies that assessed depressive symptoms rather than the criteria for major depression. These studies indicate higher rates of depressive symptoms during periods of marital disruption (8, 9); however, these studies did not determine current or past history of major depression.

In assessing the effects of marital disruption, it is important to designate the appropriate reference groups. Researchers generally combine married persons into a

single category, but evidence from community and patient samples indicates that unhappily married adults have higher rates of depression or poorer mental health than their happily married counterparts (10–14). Divorced or separated individuals may well have higher rates of major depressive episodes than happily married individuals but not higher rates than unhappily married individuals. Similarly, the short-term impact of marital disruption has to be distinguished from the longer-term consequences of life as a divorced person.

In this study, we use longitudinal data from the New Haven Epidemiologic Catchment Area (ECA) program to examine several questions about the relationship between marital disruption and risk for major depression: Are individuals undergoing marital disruption at high risk for a major depressive episode? Does marital disruption increase the risk of a first-onset major depressive episode? Are the effects of marital disruption equivalent for men and women?

METHOD

Data for these analyses were collected as part of the New Haven ECA program. The ECA program is a collaborative multistage study of the prevalence and incidence of major psychiatric disorders and the use of health and mental health services in five U.S. sites (15). Our analyses are confined to the New Haven data to take advantage of information on marital quality unique to the New Haven site.

Beginning in July 1980, 5,034 interviews (including an oversample of elderly respondents) were obtained from a multistage probability sample of adults 18 years

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old and older living in a 13-town region of the greater New Haven area. These interviews represented a response rate for the first stage of 78% ($N=5,034$); 81% ($N=4,081$) of these respondents were reinterviewed after approximately 6 months; 91% ($N=3,694$) of the second-stage respondents were interviewed approximately 6 months later. The methods used in the ECA project have been described in greater detail elsewhere (15, 16).

The objectives of this study focused on a subsample of respondents, namely, 54 respondents who reported that they separated from or divorced their legal spouses over the course of the study period. This group included subjects with three types of change of legal marital status: married subjects who separated from their spouses ($N=14$), married subjects who divorced ($N=11$), and separated subjects who divorced ($N=29$). These three subgroups were combined to increase the size of the index group of interest after initial estimates indicated that their risks of major depressive episodes were similar. To minimize age variation, one 73-year-old subject was omitted from the study, leaving 53 subjects 18–60 years old.

The index group was compared with three other groups of subjects 18–60 years old whose legal marital status did not change during the study period. The first group comprised married respondents who at the first interview reported themselves as "getting along with their spouse" ($N=708$). This group was considered happily married. The second comparison group comprised married respondents who at the first interview reported themselves as "not getting along with their spouse" ($N=259$). This group was considered unhappily married. The third comparison group comprised separated or divorced respondents whose legal status did not change over the study period ($N=205$). The duration of their marital status was not known.

The two comparison groups of married respondents were differentiated by the self-reported quality of their marriages. We used the reports only from the first interview to avoid confounding subsequent reports of marital quality with depressive status.

Diagnostic assessment was based on information gathered by lay interviewers using the National Institute of Mental Health Diagnostic Interview Schedule (DIS) (17, 18). Depressive episodes were assessed by computer algorithms using the *DSM-III* criteria of having a period of 2 weeks or more of dysphoric mood as well as symptoms from at least four of the eight *DSM-III* depression symptom groups. Respondents met criteria for major depression if they reported experiencing at least one depressive episode but no manic symptoms ever. Depressive episodes in response to bereavement were not coded as major depression unless the episode lasted a year or more.

We used unweighted data in subjects classified according to their marital status to compare rates of major depression occurring between the first and last interviews, a period of approximately 1 year. Chi-square tests generated from logistic regression models, adjusted for age, estimated the relative rates between subgroups.

Period prevalence is defined as the proportion of subjects in the total group who reported an episode of major depression between interviews. Incidence is defined as the proportion of the group at risk for first-onset major depression who reported a depressive episode between interviews. Respondents excluded from the group at risk for a first-onset major depression were 1) respondents who, at the first interview, reported either a history of major depression or a history of mania and 2) respondents who, at the subsequent interview, reported an age at onset of major depression that was younger than their age at the first interview. The latter criterion compensates for possible underreporting of past history of depression (19, 20) as well as changes in the DIS version used in the subsequent interview. This approach should minimize overinflating incidence rates because any remaining cases of unreported past history would likely be in the denominator rather than the numerator.

RESULTS

The analyses first compared the sex, age, and history of major depression of subjects in the marital disruption group and subjects in the other three marital categories. The proportion of women in the marital disruption group (29 [54.7%] of 53) was significantly lower than in the groups of separated or divorced respondents whose legal status did not change over the study period (147 [71.7%] of 205) ($\chi^2=5.84$, $df=1$, $p<0.02$) but did not differ from those in the two groups of respondents who remained happily or unhappily married during the study period. The average age (36.9 years) of the subjects in the marital disruption group did not differ from that of any of the other three groups.

Nine (31.0%) of the 29 women in the marital disruption group reported a history of major depression at the first interview, compared with 33 (8.7%) of the 379 happily married women ($\chi^2=12.39$, $df=1$, $p<0.001$) and 23 (16.4%) of the 140 unhappily married women ($\chi^2=3.22$, $df=1$, $p<0.08$). The 24 men in the marital disruption group did not differ significantly from the men in the other groups in reporting a history of major depression. However, only two of the 24 men in the marital disruption group reported a history of depression, so the statistical power to detect such differences is very low.

Over the course of study year, 63 (9.1%) of the 695 women and 26 (4.9%) of the 530 men reported an episode of major depression. The prevalence of major depression for men and women in each marital category is shown in table 1. The prevalence of major depression in the women who experienced marital disruption was 3.1 times higher than it was in the happily married women ($\chi^2=6.83$, $df=1$, $p<0.009$), 2.1 times higher than in the unhappily married women ($\chi^2=2.54$, $df=1$, $p<0.11$), and 1.7 times higher than in the women who had been divorced or separated before the study began ($\chi^2=1.47$, $df=1$, $p<0.23$). For men, the pattern was similar but more extreme; the prevalence of major depression

TABLE 1. One-Year Rates of Major Depression in Married and Unmarried Men and Women

Marital Category	Women			Men			Sex Ratio (Female:Male)
	N	Major Depression		N	Major Depression		
		N	%		N	%	
All subjects							
Happily married	379	25	6.6	329	6	1.8	3.7:1
Unhappily married	140	14	10.0	119	10	8.4	1.2:1
Divorced or separated before study began	147	18	12.2	58	6	10.3	1.2:1
Divorced or separated during study period	29	6	20.7	24	4	16.7	1.2:1
Subjects with no history of depression							
Happily married	344	11	3.2	318	1	0.3	10.7:1
Unhappily married	116	6	5.2	102	1	1.0	5.2:1
Divorced or separated before study began	103	4	3.9	47	2	4.3	0.9:1
Divorced or separated during study period	20	1	5.0	21	3	14.3	0.3:1

among the men in the marital disruption group was 9.3 times higher than it was in the happily married men ($\chi^2=11.74$, $df=1$, $p<0.001$), 2.0 times higher than in the unhappily married men ($\chi^2=1.39$, $df=1$, $p<0.24$), and 1.6 times higher than in the men who had been separated or divorced before the study began ($\chi^2=0.54$, $df=1$, $p<0.46$).

The magnitude of the differences in rates of major depression between the subjects in the marital disruption group and the happily married subjects was similar for men and women. Although the relative effect for men was about 3 times greater, the interaction with sex was not significant ($\chi^2=1.58$, $df=1$). Significant differences between men and women in prevalence rates of depression were observed only for the happily married ($\chi^2=8.39$, $df=1$, $p<0.01$).

Subjects with a past history of major depression or mania are omitted from the estimated incidence rates in the lower half of table 1. Because approximately two-thirds (60 of 89 subjects) of the subjects found to have major depression reported previous histories of depression, the remaining number of first-onset cases was too small to conduct statistical tests of significance. The trends in rates of depression for men and women, however, are worth noting. Among women who were at risk for a first episode of depression, there was little variability in rates of major depression across marital status groups. However, for men, the marital disruption group was substantially more likely to report first-onset depression than the other marital status groups.

In comparison to the happily married group ($\chi^2=4.83$, $df=1$, $p<0.05$) and the unhappily married group ($\chi^2=3.11$, $df=1$, $p<0.10$), the effects of marital disruption on the likelihood of first-onset major depression were greater for men than women. Rates of first-onset major depression were higher in women than men only among the happily and unhappily married groups.

DISCUSSION

To summarize, prevalence rates of major depression were higher among men and women experiencing mari-

tal disruption than among the happily married. Among respondents without a history of depression or mania, marital dissolution was associated with a higher risk of first-onset major depression for men but not for women. Differences between men and women in rates of major depression varied by marital status: the prevalence rates were higher for women only in the happily married group.

Although the process of separation or divorce may have substantial personal, social, and economic consequences for both men and women, this study found that the effects of marital disruption on the risk of first-onset major depression were greater for men than for women. These findings are consistent with previous studies reporting that the psychological advantages of marriage are greater for men than women (4, 21, 22), which suggests that the impact of marital disruption may be more detrimental to men. Other retrospective studies also suggest that women experience depressive episodes earlier in the process of marital disruption than men (23, 24). However, the current findings differ from reports that personal events have comparable impact on men and women (25, 26) or that divorce burdens women disproportionately with financial strains (1).

It is important to note that our study design did not allow the development of a temporal sequence of events, i.e., the timing of the marital disruption in relation to the onset of the major depressive episode. Although the New Haven study included an intervening DIS assessment, the data were too sparse to analyze three points in time. Marital disruption is not a single, acute event; the process generally develops over time, as does major depression. Indeed, much of the literature suggests that problems in marriage "trigger" (14) or are precursors (12) of depressive episodes. The assumption is that the marital disruption and depressive episode are coterminous events.

Several other limitations of this study should be noted. The number of respondents reporting marital disruption was too small to compare the risk of depression by age, for example, or by initial reports of marital happiness (preliminary estimates suggested no difference in effect by initial reports). The study was limited

to adults 18–60 years old because marital disruption is especially rare among the elderly (2, 27). Finally, this study describes the relationship only between marital disruption and major depression; other research indicates that marital disruption may also be related to other psychiatric problems such as anxiety symptoms or substance abuse (28).

There were too few respondents with a past history of depression in this study to compare recurrence rates by marital groups. However, the rate of recurrence for major depressive episodes is estimated at about 50% (*DSM-III-R*, p. 228). Even with the small subsamples, the recurrence rates in our marital disruption groups were not high (one of two men; five of nine women), nor did they seem to differ from the rest of the sample.

It is interesting to compare these findings with studies of the newly bereaved. In another ECA study, the prevalence rates of major depressive episodes were higher among newly widowed men and women than among married men and women (29). However, there was no sex difference in the effects of bereavement on the risk of a first-onset depressive episode. Newly divorced subjects were more likely to have a past personal or familial history of depression than newly widowed subjects (especially newly widowed women) (29, 30). For men, both types of losses were associated with a greater risk of a first-onset depressive episode. According to *DSM-III-R*, depressive symptoms are a normal reaction to the death of a loved one and most depressions of bereavement are not considered major depressive episodes. These exclusion criteria do not apply to marital separation or divorce. Although the etiology of the processes may differ, both marital disruption and conjugal bereavement are characterized by the loss of a spouse. Given the similarity in the nature of the two events and in their risk for depressive reactions, the application of different duration thresholds in the diagnostic criteria may be worthy of reconsideration.

The prevalence of major depression was 3.7 times higher among happily married women than among their male counterparts but comparable for all other marital categories. These patterns were even more extreme for first-onset depression. Since the happily married group was also the most common in our and other study populations, most reported sex ratios for the risk of depressive episodes in adults are weighted toward observations among the happily married. The findings from the New Haven ECA suggest that men and women facing marital dissolution should be considered at equally high risk for major depression and that, among individuals without a history of depression, marital disruption poses a greater risk for men.

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Depression in Patients With Acute Traumatic Brain Injury

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Objective: This study was undertaken to examine patients with closed head injuries for the presence of depressive disorders. **Method:** A consecutive series of 66 patients with closed head injuries but no significant spinal cord or other organ system injury were examined by means of a semistructured psychiatric interview. The Hamilton Rating Scale for Depression as well as scales measuring impairment in activities of daily living, intellectual functioning, and social functioning were administered. The patients' CT scans were also examined. **Results:** Seventeen patients had major depression and two had minor depression. The presence of left dorsolateral frontal lesions and/or left basal ganglia lesions and, to a lesser extent, parietal-occipital and right hemisphere lesions was associated with an increased probability of developing major depression. Compared to the nondepressed group, the group with major depression had a higher frequency of previous psychiatric disorder and showed evidence of poorer social functioning. **Conclusions:** Major depression occurs in about one-quarter of patients after traumatic brain injury. This is the same frequency as in other major disorders such as stroke. Major depression appears to be provoked by one or more factors that include poor premorbid social functioning and previous psychiatric disorder or injury to certain critical brain locations. (Am J Psychiatry 1992; 149:918-923)

With an annual incidence of 2 million cases, trauma is the most common cause of brain injury in the United States (1). In approximately 500,000 of these cases, the patients require hospitalization, and 80,000 have long-term sequelae of their brain injuries (1).

The observation that brain injury leads to a variety of neuropsychiatric disorders has been reported in the medical literature for many years. Adolf Meyer (2), for example, identified a number of disorders that he referred to as the "traumatic insanities," and he associ-

ated these disorders with specific lesion locations. Our knowledge about the behavioral and emotional effects of frontal lobe injury is largely the result of studying patients with traumatic brain injury. For instance, one of the best-known and earliest examples of behavioral and emotional changes associated with traumatic injury is Phineas Gage (3). His penetrating frontal lobe injury, caused by a railroad spike, led to a variety of emotional and personality changes, including disinhibition, apathy, loss of appropriate social behavior, and lability of mood.

The quantitation of severity of traumatic brain injury by Teasdale and Jennett (4) led to a large number of studies examining the neurobehavioral consequences of mild, moderate, and severe head injuries (5-7). These studies have identified numerous behavioral and emotional consequences of brain injury as well as numerous prognostic factors related to long-term outcome. There have been relatively few studies of mood disorders associated with traumatic brain injury, however, and most of these studies have used rating scales, questionnaires, or relatives' reports rather than structured mental status examinations and well-established diagnostic criteria to determine the existence of depression (8, 9).

For several years, we have been reporting on the incidence (10), phenomenology (11), course (12), and treatment (13) of mood disorders in patients with focal brain injury due to stroke. We have reported that depression occurs more frequently in patients with either

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left dorsolateral frontal cortical lesions (14) or left basal ganglia lesions than in patients with lesions in any other location (15). In addition, for both cortical and subcortical lesions, the proximity of the lesion to the frontal pole was significantly correlated with severity of depression (14).

One of the major questions, however, is whether these findings in stroke patients are generalizable to other brain-injured populations or whether there is something unique about the stroke population that contributes to the prevalence of depression. For example, compared to patients with traumatic brain injury, stroke patients tend to be older, to have potentially recurrent cardiovascular illnesses, and, frequently, to be taking multiple medications for various illnesses.

Any of these factors or other variables might influence the expression of depression and its neuropathological correlates. In addition, the nature of the brain injury is different following stroke than following trauma. Traumatic injury is associated with diffuse axonal shear injury, contusions, and both arterial and venous bleeding, while ischemic infarction and intraparenchymal hemorrhage are the neuropathological mechanisms associated with stroke.

We have conducted one previous study comparing the severity of depressive symptoms in patients who had had strokes and patients with closed head injuries (16). We found that although the stroke patients were more severely depressed than the patients with traumatic brain injury, the difference in severity of depressive symptoms was explained in large part by differences in the location of CT-visualized lesions in the left hemisphere. In addition, for both traumatic brain injury and stroke there was a significant correlation between proximity of the largest lesion to the left frontal pole and severity of depression.

In the present study, patients with acute traumatic brain injury but without multiple system injury (e.g., patients without multiple fractures or intra-abdominal lesions) were examined with the use of structured interviews and diagnostic criteria to determine whether similar lesion locations or other clinical variables would be associated with major depression.

METHOD

Sixty-six patients with acute closed head injuries who had been consecutively admitted to a shock trauma center were included in the study. Patients were excluded if they had open head injuries, spinal cord injuries, or significant multiple system injuries such as multiple fractures, rupture of the spleen, or lung collapse. In addition, patients were excluded if they had a decreased level of consciousness or aphasia that interfered with their ability to comprehend questions administered during a verbal interview (i.e., patients had to be able to follow at least a two-stage command).

Questions regarding personal and family history of psychiatric disorder were included in the structured inter-

view. Information about the existence of previous mood disorder as well as alcohol or other substance abuse, in the family history or the personal history, was specifically asked of each patient and relatives who were present at the time of interview. A psychiatric history was considered positive for a disorder if the patient or a relative appeared to meet the *DSM-III* criteria for that disorder. This diagnosis did not depend on the patient's receiving treatment. None of the patients had a depressive disorder at the time of the traumatic brain injury, and none received the head injury as a result of a suicide attempt.

After they gave informed consent, all patients received detailed psychiatric examinations approximately 1 month after injury. Symptoms of depression, mania, and anxiety were elicited with a modified version of the Present State Examination (PSE) (17) administered by a research psychiatrist (A.W.F.). This is a semistructured psychiatric interview that was modified to examine all symptoms used in the *DSM-III* criteria.

Quantitative mood ratings were obtained with the observer-rated Hamilton Rating Scale for Depression (18), a 17-item scale that measures psychological and physiological symptoms of depression. Cognitive function was measured with the Mini-Mental State examination (19), which has been shown to be a reliable and valid means of assessing a limited range of cognitive functions in several medically ill or brain-injured populations (16). Mini-Mental State scores range from 0 to 30, with scores below 24 indicative of clinically significant cognitive impairment.

Impairment in activities of daily living was measured with the Johns Hopkins Functioning Inventory (16). Scores on this scale range from 0 to 27, with higher scores indicating a greater degree of functional impairment. Social functioning was quantitatively assessed with the Social Functioning Exam and the Social Ties Checklist (20). The Social Functioning Exam, which has been shown to be reliable and valid for patients with stroke, assesses patients' satisfaction with their social functioning by means of a structured interview. Scores range from 0.00 (greatest satisfaction) to 1.00 (least satisfaction). The Social Ties Checklist assesses the number of social connections available to the patient. Scores may range from 0 to 10, with higher scores indicating less social support.

All neurological examinations were conducted by a neurosurgeon (F.H.G.) who was blind to the results of the psychiatric examinations. Results of the neurological examinations were recorded by using the standardized neurological examination form of the Traumatic Coma Data Bank (21).

CT scans were obtained as part of the standard clinical evaluation of patients admitted to the emergency medical services system that administers the shock trauma center. Scans were usually done within the first day after trauma and repeated 1–2 weeks later. All scans were done on a GE-1010 scanner with standard 10-mm axial cuts parallel to the canthomeatal line.

The nature of the lesion (e.g., contusion, intraparenchymal bleeding, subarachnoid hemorrhage) was deter-

TABLE 1. Characteristics of 64 Depressed and Nondepressed Patients With Traumatic Brain Injury

Variable	Patients With Major Depression (N=17)		Patients Without Depression (N=47)	
	N	%	N	%
Male sex	14	82.4	41	87.2
Black race	5	29.4	11	23.4
Left-handedness	1	5.9	4	8.5
Married	7	41.2	21	44.7
Hollingshead socioeconomic class IV or V	13	76.4	34	72.3
Family history of psychiatric disorder	8	47.1	23	48.9
Personal history of psychiatric disorder ^a	12	70.6	17 ^b	37.0
Personal history of alcohol and other substance abuse	8	47.1	11 ^b	23.9

^aSignificant difference between groups ($\chi^2=4.38$, $df=1$, $p=0.04$).

^bN=46.

mined from the CT scan. All scans were read by a neurologist (S.E.S.) who was blind to the results of the psychiatric examination. All lesion locations were determined and transposed onto templates according to the procedure described by Levine and Grek (22). Subjects with specific lesion locations (e.g., left anterior lesions) were defined as patients whose CT scans showed lesions in those locations (e.g., left dorsal lateral frontal cortex and/or left basal ganglia) regardless of whether lesions were also seen in other locations.

Several of the rating scale scores and other variables showed abnormal distributions. For consistency, we used nonparametric procedures throughout our statistical analyses. For instance, when we compared the depressed and nondepressed groups for differences on the demographic variables (e.g., age, sex), we used Mann-Whitney U or chi-square tests. When we analyzed scores on the six psychiatric rating scales, we conducted an overall multivariate test of significance in order to 1) account for the intercorrelations among scores on the rating scales and 2) control the overall probability of obtaining a significant result by chance (alpha error). This was accomplished with a nonparametric analog of discriminant analysis based on ranks (23). The overall test of significance was taken as the test for the full model including all scales.

Logistic regression was used to test for an association between the diagnosis of depression and lesion location. Again, an overall test was used to control for alpha inflation and interrelations among the lesion locations. Following the significant likelihood ratio test for the full model, backward selection was used to reduce the number of lesion locations considered.

RESULTS

Seventeen subjects met the *DSM-III* symptom and duration criteria for major depression, and 47 had no

diagnosis of mood disorder. Two additional patients met the *DSM-III* symptom criteria for dysthymia (we have referred to this as minor depression), but their data were excluded from further analysis because of the small number in this category. The depressed subjects' mean age was 26.8 years ($SD=5.8$), and the mean age of the subjects without mood disorder was 29.5 ($SD=10.7$). The mean number of years of education was 12.4 ($SD=2.0$) for the depressed group and 12.3 ($SD=2.1$) for the rest of the subjects. The time from injury to interview was 36.6 days ($SD=15.8$) for the depressed patients and 32.1 days ($SD=20.7$) for the patients without mood disorder. Other background characteristics of the study population are shown in table 1.

There were no significant differences between the depressed and nondepressed groups in terms of age, sex, race, marital status, education, socioeconomic class, or medication taken at the time of interview. The study group consisted primarily of men in Hollingshead's socioeconomic class IV who were in their late 20s. There were no significant differences between the depressed and nondepressed patients in the frequency of a past family history of psychiatric disorder.

There was a significantly greater frequency of a previous personal history of psychiatric disorder in the group with major depression (table 1). When patients with histories of alcohol or other substance abuse were excluded, this difference was no longer significant. There was no significant difference between groups in the frequency of a personal past history of alcohol and/or other substance abuse.

There were no significant differences between the two groups in the frequency of any neurological findings. Twenty-six patients (seven with major depression and 19 without depression) had some motor impairment, 13 (seven depressed and six nondepressed) had sensory impairment, and 14 (three depressed and 11 nondepressed) had ocular palsies. Only one of the 17 patients with major depression and four of the 47 nondepressed patients were given a diagnosis of Broca's or Wernicke's aphasia. In the remaining patients who presented with language impairment (five depressed and 14 nondepressed), there was mild global aphasia, transcortical sensory or motor aphasia, or severe anomia.

The Glasgow coma scale scores 24 hours after injury were not significantly different between groups (depressed patients, mean=9.2, $SD=3.4$; nondepressed patients, mean=10.0, $SD=3.4$), nor was there a significant difference in the distribution of mild head injury (Glasgow coma score=12–15; 35% of the depressed and 43% of the nondepressed patients), moderate head injury (Glasgow coma score=8–11; 24% of the depressed and 26% of the nondepressed patients), or severe head injury (Glasgow coma score=3–7; 41% of the depressed and 32% of the nondepressed patients).

Multivariate discriminant analysis showed an overall significant difference between the group with major depression and the nondepressed group in psychiatric rating scale scores (Wilks's lambda=0.38, $F=15.4$, $df=6$, 56, $p=0.0001$). Univariate test statistics disclosed sig-

TABLE 2. Scores on Psychiatric Rating Scales of 64 Depressed and Nondepressed Patients With Traumatic Brain Injury

Scale	Score				Analysis	
	Patients With Major Depression (N=17)		Patients Without Depression (N=47)		F (df=1, 61)	p
	Mean	SD	Mean	SD		
Hamilton Rating Scale for Depression	13.8	3.2	6.8	2.6	37.79	0.0001
Present State Examination	19.6	4.2	6.8	3.6	78.70	0.0001
Mini-Mental State	27.5	2.3	26.5	3.1	1.74	0.19
Johns Hopkins Functioning Inventory	2.2	3.3	1.4	1.8	0.31	0.58
Social Ties Checklist	4.2	1.2	3.6	1.5	2.49	0.12
Social Functioning Exam	0.19	0.16	0.11	0.10	4.92	0.03

nificant between-group differences in Hamilton depression scores, PSE scores, and Social Functioning Exam scores (table 2). There were no significant intergroup differences in intellectual impairment as measured by the Mini-Mental State examination, impairment in activities of daily living as measured by the Johns Hopkins Functioning Inventory, or social connectedness as measured by the Social Ties Checklist.

According to the resulting discriminant function, 18 (29%) of 63 patients were classified into the depressed group and 45 (71%) were classified into the nondepressed group (three patients were excluded from the analysis because of missing data). These findings indicate a 100% sensitivity and a 98% specificity.

Of the 47 nondepressed patients, 41 had abnormal findings on CT scans, and of the 17 patients with major depression, 15 had CT scan abnormalities. Of the total of 56 subjects who exhibited abnormal CT scans, 22 had single focal lesions and 23 had multiple or bilateral lesions. In addition, 13 patients had extraparenchymal hemorrhages (epidural, subdural, or subarachnoid bleeding) or CT evidence of brain edema, brain atrophy, or hydrocephalus. Most of the patients (71% of the depressed and 62% of the nondepressed patients) had CT evidence of brain contusions. There were no significant differences in the frequency of various types of injury between the depressed and nondepressed groups.

To analyze the relation between lesion location and the presence of major depression, a logistic regression model was used. The model included the following location variables: left hemisphere, right hemisphere, cortical, subcortical, single, multiple, frontal, orbitofrontal, temporal, temporobasal, left anterior (i.e., left dorsolateral frontal cortex and/or left basal ganglia), and parietal-occipital. There was an overall significant association between lesion location and the development of major depression ($\chi^2=33.64$, $df=12$, $p=0.0008$). A backward selection procedure was used to remove the nonsignificant variables ($p>0.05$). After their removal, the reduced model included the following lesion locations: left hemisphere only, right hemisphere only, cortical, frontal (i.e., right, left, or bilateral frontal excluding orbitofrontal involvement), left anterior, and parietal-occipital ($\chi^2=31.39$, $df=6$, $p=0.0001$).

The parameter estimates and probabilities of each of

TABLE 3. Maximum Likelihood Estimates for Regression Coefficients of Lesion Locations and Depression in 64 Patients With Traumatic Brain Injury

Lesion Location	Parameter Estimate	Standard Error	Analysis	
			Wald χ^2 (df=1)	p
Left hemisphere	-2.84	1.44	4.08	0.04
Right hemisphere	2.40	1.12	4.74	0.03
Cortical	-3.67	1.45	6.28	0.01
Frontal	-3.58	1.38	6.56	0.01
Left anterior	5.90	1.64	12.97	0.0003
Parietal-occipital	3.75	1.44	6.91	0.009

these six individual variables are shown in table 3. The presence of a left anterior lesion was by far the strongest correlate of major depression. To a lesser degree, parietal-occipital and right hemisphere lesions increased the probability of developing major depression. On the other hand, the presence of left hemisphere, cortical, and frontal lesions was associated with a decreased probability of developing major depression. If we compare the predicted and observed events, the model shows a 70% sensitivity and an 83% specificity.

DISCUSSION

This study for the first time examined patients with traumatic brain injury for depressive disorder with the use of a structured psychiatric interview and *DSM-III* diagnostic criteria. We found that 27% of the patients whose data were analyzed met the criteria for major depression. This frequency is within the wide frequency range for depression reported by other investigators who have used cutoff scores on self-rated depression scales (8) and is close to the frequency of major depression found in patients with stroke (10). Perhaps the failure to use structured psychiatric interviews and defined diagnostic criteria is the reason that the reported frequency of depression following traumatic brain injury has varied from 10% to 60% (24).

This study also found that major depression following traumatic brain injury was significantly associated with lesion location. The presence of left anterior lesions (i.e., left dorsolateral frontal and/or left basal gan-

glia lesions) and, to a lesser degree, parietal-occipital and right hemisphere lesions was associated with a higher probability of developing major depression. On the other hand, the presence of left hemisphere lesions, frontal (i.e., right, left, or bilateral frontal excluding orbitofrontal) lesions, and purely cortical lesions diminished the probability of developing a major depressive disorder. A previous personal history of psychiatric disorder (including alcohol and other substance abuse) was more frequent in the group with major depression. This group also showed evidence of poorer premorbid social functioning.

Before further discussion of this study, several methodological limitations should be acknowledged. First, only patients who were alert and cognitively able to be interviewed were included. Second, only patients with relatively minor injury to other body systems were included, so that a more uniformly injured population, without major disability due to non-CNS injury, could be studied. In addition, the patients were primarily young white men from the lower socioeconomic classes who had histories of alcohol or drug abuse. Although this demographic profile is typical of the population reported in epidemiologic studies of traumatic brain injury (1), our findings may not be applicable to all patient populations with traumatic brain injury. Closed head injuries involve trauma to the entire brain, and it would be misleading to assume that the only areas that have been injured are the ones visible on CT scan.

While it is certain that the extent of brain injury was underestimated in this study (we did not have information from magnetic resonance imaging), it is unlikely that there was any systematic underrepresentation among patients who met the criteria for major depression, since the mean scores on the Glasgow coma scale, the Johns Hopkins Functioning Inventory, and the Mini-Mental State examination and the distribution of mild, moderate, and severe head injuries were not significantly different between groups. In addition, we did not examine the patients for neglect, disturbances in prosody, unawareness of deficits, or denial of illness (disturbances that are usually associated with right hemisphere lesions). It is possible that some patients with these disturbances may not have been able to recognize their inner mental state appropriately.

Given these cautions, what are the implications of this study? First, the study supports our previous finding in patients with stroke of an increased frequency of depression among those with left dorsolateral cortical and left basal ganglia lesions (14, 15). This finding is consistent with a previous study of patients with chronic brain injuries in which anterior left hemisphere lesions were found to be associated with the most severe depressive symptoms in both stroke and traumatic brain injury (16). It is interesting that the association between major depression and left anterior lesions was highly significant despite the "protective" effect associated with the presence of both left hemisphere and frontal lesions. This finding suggests that the left dorsolateral frontal cortex and the left basal ganglia are critical structures in the left hemisphere as far as mood is con-

cerned, and they may represent strategic lesion locations for the initiation of major depression. The probability of developing major depression was also associated with the presence of parietal-occipital lesions and with the presence of right hemisphere lesions.

Grafman et al. (25) reported that depressive symptoms were associated with penetrating injuries that involved the right hemisphere (right orbitofrontal lesions). Their subjects, however, were studied years after the penetrating injuries, without the use of structured psychiatric interviews, and are not comparable to the patients in this study. Lishman (26) also reported that several years after penetrating brain injury, depressive symptoms were more common among patients with right hemisphere lesions. We previously examined the correlates of depression following acute-stroke lesions of the right hemisphere (27). Patients who developed major or minor depression during the in-hospital evaluation for acute stroke had a higher frequency of parietal lobe lesions than the nondepressed or unduly cheerful patients. Finset (28) reported the occurrence of depression following right hemisphere parietal lobe damage. In the present study, we also found that purely cortical lesions were associated with a decreased probability of developing major depression. This indicates that subcortical and basal ganglia lesions may have the strongest correlation with major depression.

We have previously suggested (14) that the mechanism of depression following anterior brain injury may involve the interruption of biogenic amine-containing neurons as they pass through the basal ganglia or frontal subcortical white matter. This hypothesis remains consistent with our findings in the present study.

This study also suggests that premorbid vulnerability factors (personal history of psychiatric disorder and poor social functioning) may be operative in the development of major depression among patients with traumatic brain injury. This is consistent with our findings and those of other investigators in stroke and traumatic brain injury (10, 29) and suggests several areas for further investigation.

Although other investigators have not found that severity of depressive symptoms is significantly correlated with duration of loss of consciousness, duration of post-traumatic amnesia, or the presence of skull fracture (9), depression following traumatic brain injury has been associated with degree of neuropsychological impairment (9). We did not find a significant difference in degree of intellectual impairment between our depressed and nondepressed patients. This may be because we examined less severely injured patients (the mean Mini-Mental State examination scores for depressed and nondepressed patients were 27.5 and 26.5, respectively), and there may have been a "ceiling" effect that precluded demonstrating an influence of depression on intellectual function.

The finding of relatively low Hamilton depression scale scores among the patients with major depression is another important issue. Although these total depression scores were not significantly different from those

we found previously among patients who developed major depression following stroke or myocardial infarction (30), we are examining this issue in more detail in another study (i.e., examining which symptoms are specific to depression following traumatic brain injury). Several facts, however, should be kept in mind. First, the diagnosis of depression was based on meeting the *DSM-III* criteria for depression and was made by research psychiatrists using a semistructured interview. This remains the "gold standard" for depression, and all of the patients met these criteria. Second, the patients were identified on the basis of the existence of traumatic brain injury and not depression and therefore might not have had symptoms as severe as those found in patients at psychiatric institutions. Moreover, the patients with traumatic brain injury who had major depression had Hamilton depression scores that were highly significantly different from those of the nondepressed patients. Third, depressive symptoms included in the Hamilton scale but not used by *DSM-III* for diagnosis may be somewhat different in functional depression and traumatic brain injury depression, and subgroups of patients with traumatic brain injury may be identified on the basis of the presence of different symptom profiles or longitudinal course.

There are probably multiple etiologies for depression after traumatic brain injury. Some may involve single etiologic agents (e.g., genetic factors), while others may involve a complex interaction between organic and psychosocial factors. Moreover, even within the group with lesions in certain critical brain regions, the phenomenology and the pathophysiological mechanisms of depression may be different (e.g., following left anterior as compared with right parietal lesions).

Future studies will need to examine a variety of outcome variables, including the course of these depressions, the dynamic changes in their clinical correlates, their effect on recovery from traumatic brain injury, their etiology, and their response to treatment. These kinds of investigations may ultimately facilitate the early recognition and treatment or prevention of these severe mental disorders.

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Regional Cerebral Blood Flow in Childhood Autism: A SPECT Study

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Objective: The authors investigated a possible cortical brain dysfunction associated with infantile autism. **Method:** They measured regional cerebral blood flow with single photon emission computed tomography (SPECT) and xenon-133 in 21 children with primary autism (according to DSM-III-R criteria). Five cortical brain areas including frontal, temporal, and sensory association cortices were examined in order to test the recent hypothesis of cerebral dysfunction in primary autism. Anatomical references for each subject were obtained with computerized tomography or magnetic resonance imaging and were used to delimit the regions of interest for SPECT analysis. **Results:** When the results from the group with primary autism were compared with an age-matched group of nonautistic children with slight to moderate language disorders (N=14), no cortical regional abnormalities were found. **Conclusions:** It appears that there is no regional cortical dysfunction in primary autism; however, in light of methodological limitations, one cannot exclude the possibility of more localized or subcortical brain dysfunctions in autism.

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Childhood autism is an early and severe developmental disorder characterized by deficits in verbal and nonverbal language and social and cognitive functioning (1; DSM-III-R). Little is known about the neurobiological mechanisms that could underlie this disorder. Brain morphological investigations with computerized tomography (CT) scans in autistic subjects have shown reversed cerebral asymmetries (2) and enlargement of the lateral and third ventricles (3, 4), but failed to find a consistent abnormal pattern in the disorder. Some, but not all, magnetic resonance imaging (MRI) studies have reported a hypoplasia of the cerebellar vermis (5, 6), enlargement of the fourth ventricle (7), and cortical abnormalities compatible with developmental malformations, such as polymicrogyria and macrogyria (8). Although these results strengthen the

hypothesis of brain dysfunction in autism, many questions remain unanswered concerning the localization and the nature of these dysfunctions. In addition, an abnormal process of brain maturation that could lead to autism has yet to be identified.

An in vivo approach to brain function is now available with positron emission tomography (PET) and single photon emission computed tomography (SPECT), which could provide additional information about the autistic disorder. Measurements of regional cerebral blood flow (rCBF), coupled with measurements of brain metabolism at rest (9), permit the study of regional brain activity and could be helpful in localizing a regional brain dysfunction in autism. In addition, the changing metabolic patterns accompanying brain development during normal childhood have been determined (10), opening the way to the investigation of brain maturation in autism. To our knowledge, only three PET studies of cerebral glucose metabolism have been reported in autistic subjects (11-13), and they failed to detect regional abnormalities. Those studies were performed either in adults or in children with a wide age range, and the results were compared with adult values. We believe that functional brain studies of children could be more helpful than those of adults because autistic signs are more pronounced during childhood. In addition, restricting the age range of the children and using an age-matched comparison group

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TABLE 1. Clinical Characteristics and Individual Cortical Cerebral Blood Flow (CBF) Values of Autistic Children

Subject	Age (years)	Behavioral Score ^a (0-116)	Language Score ^a (1-5)	Developmental Score ^a (1-5)	Neurological Score ^a (1-5)	Mean Cortical CBF (ml/100 g/min)
1	7	27	2	1	1	67.9
2	5	35	4	1	1	89.0
3	5	65	4	4	2	89.4
4	11	67	4	4	1	53.3
5	6	47	3	4	1	74.1
6	7	46	3	4	2	70.3
7	11	63	4	5	2	58.4
8	9	44	4	4	2	73.3
9	7	34	5	4	2	51.1
10	8	51	4	5	2	78.4
11	11	17	2	1	2	78.7
12	6	40	2	3	2	71.2
13	7	41	4	4	2	69.0
14	8	60	5	4	2	65.3
15	11	24	5	1	1	64.4
16	6	48	4	3	1	57.7
17	7	29	2	2	2	75.3
18	7	73	5	5	1	65.9
19	5	60	3	4	2	68.5
20	6	41	4	4	1	64.5
21	6	27	3	3	2	51.7
Mean	7.4	44.7	3.6	3.3	1.6	70.2
SD	2.0	15.6	1.0	1.3	0.0	10.0

^aBehavioral score: total score from 29 items; 0=absence of symptoms, 116=maximum severity. Language, developmental, and neurological scores: 1=absence of signs or normal development, 5=maximal severity of signs or severe retardation.

should contribute further to our understanding of brain maturation processes in autism. In the present study we used SPECT and xenon-133, a noninvasive technique appropriate to the study of children, to measure rCBF in 5-11-year-old children with primary autism and compared the results to an age-matched group of nonautistic children.

METHOD

Subjects

Twenty-one children, 12 boys and nine girls, with primary autistic disorder were selected among patients attending a day-care child psychiatry unit of a university hospital. Children from 5 to 11 years of age were included. The mean age was 7.5 years (SD=1.7), and the mean nonverbal IQ was 36.0 (SD=18.5) (range=10-75). Infantile autism was diagnosed according to the criteria in *DSM-III-R*. In order to select children who presented strictly primary autism, we excluded subjects with any of the following criteria: 1) known infectious, metabolic, or chromosomal disease, 2) persistent seizures, 3) identifiable neurological syndromes or focal signs, 4) abnormal EEG, and 5) abnormal CT scan or MRI, except for findings previously described in autism such as moderate ventricle enlargement or hemisphere asymmetry (2, 7). All patients were free of medication for at least 1 month before the SPECT examination.

Each child received an extensive evaluation, including a detailed developmental psychiatric history that used a videotaped psychiatric assessment, psychological and

linguistic tests, pediatric and neurological examination, and audiological assessment. Behavioral, cognition, language, and neurological signs found in each patient are listed in table 1. They were scored according to four different scales previously developed in our laboratory. The Behavior Summarized Evaluation Scale (14) evaluates both autistic symptoms and associated features including eating, sleep, and motor disorders. The development quotient evaluates the cognitive level (15), and development quotient values were classified in five levels of increasing severity: 1) development quotient more than 70, 2) 50-69, 3) 35-49, 4) 20-34, and 5) less than 20. A neurological examination and an electrophysiologic recording (EEG) enabled us to define five levels of neurological involvement (16): 1) no neurological signs, 2) minor signs and/or history of convulsions, 3) unique lesional syndrome and/or paroxysmal anomalies on the EEG, 4) multiple lesional syndromes and/or convulsive seizures, and 5) major impairments or consciousness disorders. Children with a score greater than 2 were excluded from this protocol. Speech disorders were also classified into five levels of increasing intensity (17): 1) appropriate and communicative speech, 2) minor speech abnormalities, 3) moderate speech abnormalities, 4) intense abnormalities of speech, and 5) no communicative speech.

Since rCBF studies are not performed in normal children in our institute for ethical reasons, we selected a group of 14 children, 10 boys and four girls, whose age matched the autistic group and who had undergone a SPECT examination for a slight-to-moderate language disorder, diagnosed as a developmental language disorder (*DSM-III-R* criteria). Their mean age was 8.7 years

(SD=1.5), and the mean nonverbal IQ was 96.1 (SD=12.3) (range=80–125). They had a slight scholastic retardation but did not have behavioral, social impairment, or intelligence deficits.

This study was approved by our ethical committee, and all examinations were performed with the informed consent of the parents.

Procedure

Brain imaging protocol. Brain imaging studies consisted of SPECT and CT or MRI images acquired on the same day for each subject. Performing these studies on the same day ensured that the subject's head was identically positioned for the two examinations by the same investigator. The detailed information from the CT or MRI images allowed us to perform an individual anatomical localization of brain regions in functional SPECT image analysis processes (18).

Functional images. The rCBF measurements were performed with a brain-dedicated SPECT system (Medimatic, Tomomatic 564), using a 1-minute xenon-133 inhalation (740 MBq/liter) and a 4.5-minute image acquisition (19). Autistic children were studied at sleep after premedication (rectal administration of 4 mg/kg of pentobarbital and intramuscular injection of 0.1 mg/kg of droperidol), while comparison children were studied at rest without premedication. Five 20-mm-thick contiguous axial rCBF slices were obtained with an in-plane resolution of approximately 14 mm, and three of these were used in this study (40, 60, and 80 mm above the orbitomeatal line).

Anatomical images. Anatomical images were acquired on an X-ray CT (CT, CGR 9000) for each subject. The CT imaging protocol consisted of ten 9-mm-thick slices acquired parallel to the orbitomeatal line. In addition, four of the autistic children had an MRI brain study (General Electric, MRMAX 0.5T). In these subjects, T₁ sequences were performed and 10 axial slices, 10 mm thick, were obtained.

Regions of interest. Five cortical brain regions from each hemisphere were a priori retained for analysis, on the basis of Mesulam's model of modular and hierarchical cortical organization (20): sensorimotor (including Brodmann's areas 1, 2, 3, 4, and 43 and Broca's area on the left side), visual unimodal association (including Brodmann's areas 20, 21, and 37), auditory unimodal association (Brodmann's area 22, including Wernicke's area on the left side), heteromodal association (Brodmann's areas 7, 39, and 40), and frontal (Brodmann's areas 10, 44, 45, and 46) areas. These cortical brain regions were determined on the three slices of CT or MRI images that corresponded to the levels of the SPECT images. On each CT or MRI slice a 20-mm-thick cortical ribbon was delineated and cut into regions of interest corresponding to the various cortical brain areas; Matsui's anatomical human brain atlas was used for reference (21). The entire set of regions of interest was copied onto the corresponding SPECT slice for rCBF computation, and the rCBF was averaged over

regions of interest belonging to the same cortical brain region on different slices (figures 1 and 2). Depending on the region and on subject head size, a given region could be present on one or more slices, for example, three slices for the frontal cortex and two for the sensorimotor area. This method of region of interest placement has a high interobserver reproducibility with regional intraclass correlation coefficients ranging from 0.973 to 0.995 (18). We did not include subcortical regions in the analysis because of the limitations of attenuation correction with SPECT.

Data Analysis

Mean cortical CBF was calculated as the mean CBF value of the entire cortical ribbon in the three slices. Cortical CBF and rCBF were calculated in absolute values (ml/100 g per minute). The relative values were determined as the regional values divided by the mean cortical CBF (rCBF/cortical CBF). Right-to-left ratios were defined for each region and for the cortical CBF. An anterior-to-posterior ratio was defined as the frontal value divided by posterior rCBF values (heteromodal association and visual unimodal association regions). Statistical analyses were performed on both absolute and relative rCBF values by Student's *t* test in the large cortical brain regions and in each smaller "within-plane" region of interest. In addition, right-to-left and anterior-to-posterior regional indices were analyzed in both groups with paired *t* tests. Correlations among age, clinical features (behavioral, cognitive and language scores), CBF values (regional, mean cortical), and CBF index (right-to-left and anterior-to-posterior ratios) were studied by nonparametric regressions.

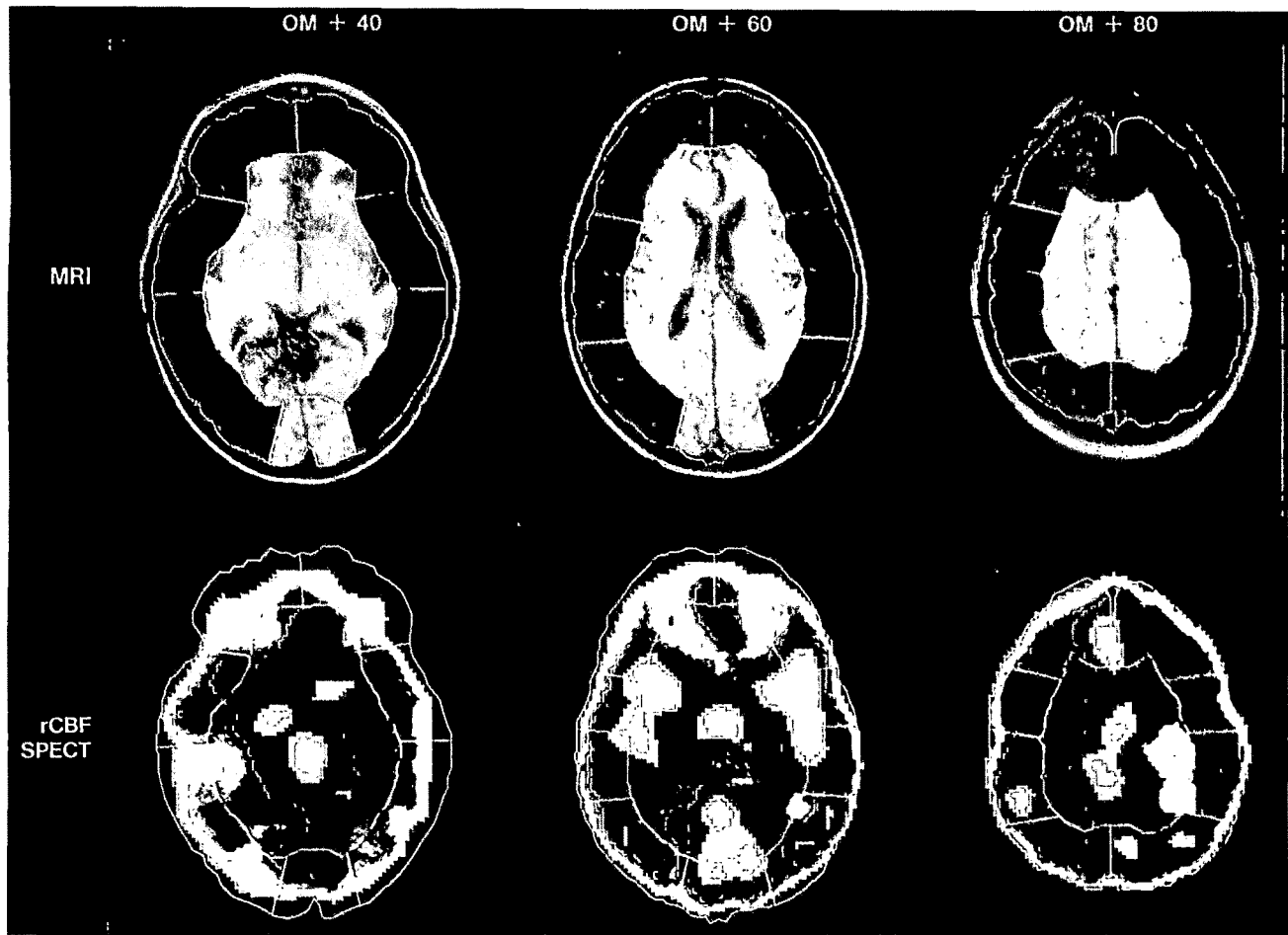
Effect of Premedication

The effect of the premedication used to sedate the autistic children was previously assessed in 10 children with neurological disorders. CBF was measured in each of these children on the same day, before and after premedication. Analysis were performed in 10 right and six left hemispheres without CBF abnormalities (four left hemispheres were excluded because of major hypoperfusion). No statistically significant difference was observed between the mean hemispheric CBF before (65.2 ml/100 g per minute, SD=8.8) and after (68.6 ml/100 g per minute, SD=10.7) premedication (paired *t* test). No effects on absolute or relative rCBF values were observed. The mean differences in relative rCBF values before and after premedication ranged from -2% (SD=3.3%) in the left visual unimodal association region to 4.2% (SD=3.2%) in the right heteromodal association region (n.s., Bonferroni's corrected paired *t* test).

RESULTS

Mean cortical blood flow was 70.2 ml/100 g per minute (SD=10.0) in the autistic group and 70.2 ml/100 g

FIGURE 1. Regions of Interest Defined on MRI Images (top) and Registered on Corresponding SPECT Slices (bottom) for 21 Autistic Children and 14 Comparison Children



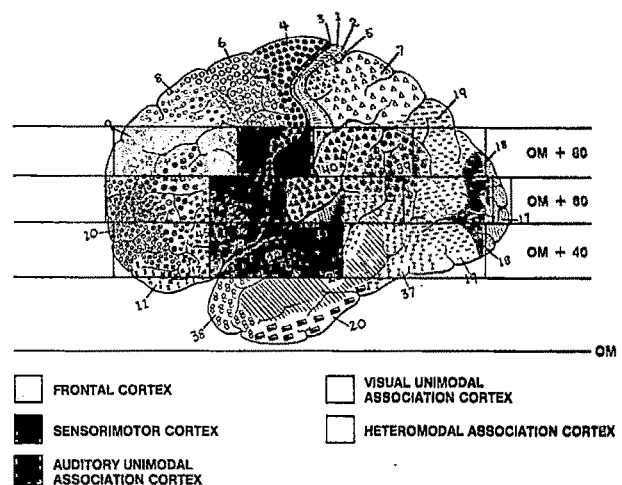
per minute ($SD=9.5$) in the comparison group. In all regions CBF values were also very similar in autistic and comparison children (table 2). Mean cortical CBF and rCBF did not correlate with age in either the autistic children or the comparison group.

No statistically significant group differences were found for relative values of rCBF (rCBF/cortical CBF) (table 2). Right-to-left and anterior-to-posterior regional indices were similar in autistic and comparison children (tables 3 and 4). No correlation was found among relative CBF values, right-to-left or anterior-to-posterior regional indices, and the clinical features analyzed (behavioral, cognitive, and language scores). Analyses performed on the smaller within-plane regions of interest also failed to reveal any statistically significant abnormalities (data not shown).

DISCUSSION

By measuring rCBF with SPECT and xenon-133 in 21 highly selected children with primary autism, we found no evidence of localized brain cortical dysfunction or abnormal index of brain maturation in this disease;

FIGURE 2. Lateral View of Brain Illustrating Pooling of Regions of Interest Into Five Cortical Brain Regions



rCBF values of autistic children at rest were remarkably similar to those of 14 nonautistic children. Previous

TABLE 2. Absolute and Relative Values of Regional Cerebral Blood Flow (rCBF) in Autistic and Comparison Children

Region	Absolute rCBF (ml/100 g/min)				Relative rCBF			
	Autistic (N=21)		Comparison (N=14)		Autistic (N=21)		Comparison (N=14)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Frontal								
Left	62.9	7.8	62.6	8.6	0.90	0.05	0.89	0.03
Right	63.1	9.0	63.0	9.6	0.90	0.06	0.89	0.05
Auditory associative unimodal								
Left	77.0	13.1	66.5	10.9	1.09	0.10	1.09	0.08
Right	79.5	10.9	77.1	10.3	1.13	0.10	1.10	0.09
Visual associative unimodal								
Left	62.6	10.6	64.8	9.6	0.88	0.05	0.92	0.05
Right	79.5	10.9	77.1	10.3	0.92	0.05	0.94	0.05
Sensorimotor								
Left	77.2	10.3	77.1	9.5	1.10	0.06	1.10	0.05
Right	80.2	12.9	79.2	9.4	1.14	0.07	1.13	0.06
Heteromodal associative								
Left	75.4	12.6	76.6	11.7	1.07	0.06	1.08	0.04
Right	79.6	13.9	77.4	12.2	1.13	0.07	1.10	0.09

TABLE 3. Right-to-Left Ratios of Regional Cerebral Blood Flow in Autistic and Comparison Children

Region	Autistic (N=21)		Comparison (N=14)	
	Mean	SD	Mean	SD
Frontal	1.00	0.05	1.00	0.05
Auditory associative unimodal	1.03	0.09	1.01	0.07
Visual associative unimodal	1.04	0.07	1.02	0.06
Sensorimotor	1.03	0.07	1.03	0.08
Heteromodal associative	1.03	0.07	1.01	0.07

TABLE 4. Anterior-to-Posterior Ratios of Regional Cerebral Blood Flow in Autistic and Comparison Children

Region	Autistic (N=21)		Comparison (N=14)	
	Mean	SD	Mean	SD
Frontal/visual				
Associative unimodal left	1.01	0.11	0.96	0.05
Associative unimodal right	0.98	0.10	0.95	0.09
Frontal/heteromodal				
Associative left	0.84	0.07	0.82	0.04
Associative right	0.79	0.07	0.81	0.06

PET measurements of glucose brain metabolism in autistic subjects also failed to find any regional cerebral abnormalities. Rumsey et al. (11) found that glucose utilization was significantly elevated in widespread regions of the brain of 10 adult autistic subjects, but no consistent localized abnormalities were identified. Horwitz et al. (13) confirmed these results but described significantly fewer large positive correlations between pairs of regions in frontal and parietal lobes in 14 adult autistic patients than in an age-matched control group. The only PET study performed in autistic children, from 2 to 18 years of age, reported a normal regional distribution of brain glucose metabolism when compared with adults (12).

The present data not only confirm but also extend those results for the following reasons. First, the global and regional CBF values in a large group of 5–11-year-old autistic children were similar to those of an age-matched comparison group but were significantly higher than those of normal young adults (mean age=22 years) studied with the same technique in our laboratory (51.0 ml/100 g per minute, SD=7.7) (Raynaud et al., unpublished data) and previously described by others (22). It is interesting that the mean CBF values in the present study (autistic group: 70.2 ml/100 g per minute, SD=10.0; comparison group: 70.2 ml/100 g per

minute, SD=9.5) are extremely close to those reported in normal 7–15-year-old children (71.0 ml/100 g per minute, SD=9.9) (23). These data confirm the finding that CBF is higher in children than in adults, as is cerebral glucose metabolism (12; Raynaud et al., in preparation) and may indicate that the maturation process responsible for a transient CBF increase during childhood is not altered in autistic children. Chugani et al. (10) showed that regional distribution of glucose metabolism is also age dependent in early childhood but that the adult pattern is present from the age of 1 year.

Second, three hypotheses of brain dysfunction in autism are largely supported by clinical, cognitive, neurophysiological, and neuroradiological data: a frontal dysfunction (24–26), a left-right asymmetry (27, 28), and abnormalities in cortical areas specialized in the processing of sensorial information (29–31). In order to test these hypotheses, we a priori chose to pool regions of interest into larger brain areas on the basis of the modular and hierarchic organization of the cerebral cortex proposed by Mesulam (20). In addition, regions of interest were determined on individual CT or MRI images to ensure accurate localization of our regional CBF measurements. We believe our method is of particular importance in studies of children, since the direct placement of regions of interest

on CBF images can be more problematic than in adults because of the difficulty in delimiting cortical borders. However, this method risks missing smaller focal areas of abnormalities. Yet, such abnormalities were not detected in the autistic or in the comparison group by blind visual analysis of individual images. Furthermore, the quantitative analysis performed on smaller within-plane regions of interest did not reveal any significant abnormalities.

Third, the present data obtained in children with primary autism constitute a valuable foundation for investigating the potential diagnostic value of SPECT for the detection of secondary autism. This is of particular interest considering the recent report of prefrontal and temporoparietal hypoperfusion in seven girls with Rett's syndrome (32), a condition that is still often misdiagnosed as primary autism.

The results of the present study, however, must be considered in the light of some technical and methodological limitations. The relatively poor spatial resolution of our device precludes a valid analysis of small brain areas that might be of crucial importance in autism. For example, the cerebellar cortex, especially the cerebellar vermis, which has been associated with autism (6), cannot be clearly distinguished from the occipital cortex in children because of a partial volume effect. Similarly, rCBF in internal temporal structures such as hippocampus and amygdala, which are of primary importance in the final integration of sensorial information and in behavior elaboration (33), could not be measured. Further, we did not analyze subcortical structures because of the lack of correction for auto-attenuation, a current technical limitation of SPECT.

For ethical reasons we do not measure rCBF in normal children in our institution. Therefore, we had the choice of using comparison values obtained from either a highly selected group of subjects with a different developmental disorder or a less homogeneous group of nonautistic children studied for various neurological signs. For these reasons, we selected as comparison subjects a group of children with mild language disorders. First, comprehensive comparisons between autistic and dysphasic children have shown marked clinical differences between both groups. Thus, it seems unlikely that an identical developmental abnormality is involved in both pathologies (34). Second, although rCBF measurements in children with language disorders show an rCBF pattern different from that of normal children (22, 35), a careful examination of published data shows that most abnormalities are apparently related to attention deficit disorder (a feature that was excluded in our dysphasic children) rather than to the language deficits. In addition, the abnormalities described are quantitatively moderate and localized primarily in subcortical structures. Since our group of children with mild language disorder participated in an independent research protocol carried out at the same time as the present work, these children were also screened to exclude any other neurological or psychiatric disorders. Consequently, we believe that our comparison of autistic and

dysphasic children should have detected rCBF abnormalities specifically related to autism.

Finally, the possible effects of the premedication administered to the autistic children but not to the comparison subjects was examined, since many sedative drugs are known to decrease CBF and cerebral metabolism (36, 37). One might speculate that the premedication might have masked elevated CBF values, which could be expected since an increase in global cerebral glucose utilization has been reported in adult autism (11). However, this remains unlikely because we found that the premedication did not alter CBF in children.

In summary, rCBF values measured at rest were normal in 5–11-year-old primary autistic children. This furnishes a basis for the future investigation of secondary autism with SPECT. It does not, of course, rule out brain abnormalities that may become detectable in the near future through use of more sophisticated stimulation rCBF studies or more specific neurochemical tracers.

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Predictors of Posttraumatic Stress Disorder After Burn Injury

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Objective: The authors' goal was to examine subjective and objective predictors of post-traumatic stress disorder (PTSD). **Method:** Hospitalized burn patients were assessed 1 week after injury with both objective predictors (percent of burned area and facial disfigurement) and subjective predictors (emotional distress and perceived social support). The patients were then assessed 2, 6, and 12 months later for development of PTSD. **Results:** Among 51 patients, 18 (35.3%) met PTSD criteria at 2 months. High rates of PTSD were also found at 6 months (N=16, 40.0% of the 40 available patients) and 12 months (N=14, 45.2% of the 31 available patients). PTSD was predicted by subjective variables assessed at baseline, but patients with more severe burns were not more likely to develop PTSD. **Conclusions:** The DSM-III-R diagnosis of PTSD relies on an objective evaluation of the stressor's severity. The prospective data in this study support those who argue that evaluations of the severity of the stressor might also take into account subjective factors.

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Although the emotional effects of severe trauma were recognized by Charcot, Freud, Janet, and others, the diagnosis of these effects has been inconsistently defined (1-3). In *DSM-I*, "gross stress reaction" excluded patients with other psychopathology, *DSM-II* deleted this category altogether, and *DSM-III* introduced explicit criteria for posttraumatic stress disorder (PTSD), but then *DSM-III-R* narrowed the stressor criterion and added that the symptoms must have a duration of at least 1 month.

One reason for this inconsistency has been the paucity of prospective data. Most studies have not assessed subjects immediately after the trauma and instead have evaluated symptomatic groups months or years after the stressful event. Such methods not only raise questions about sample bias and retrospective reporting but also preclude determining if the development of PTSD is related to the individual's emotional state at the time of the trauma. Further, studies have not quantified the stressor to determine if its severity predicts PTSD.

The DSM-IV Task Force is considering whether the current criteria for PTSD should once again be modified, especially regarding the definition of the stressor criterion. The *DSM-III* criterion ("a recognizable stressor that would evoke significant symptoms of distress in almost everyone") may have been too broad

and may have trivialized the concept, whereas the *DSM-III-R* criterion ("an event outside the range of usual human experience") may be so narrow that it wrongfully excludes some patients with posttraumatic symptoms. Also at issue is whether the stressor criterion should include an assessment of the individual's subjective response to the trauma, such as emotional distress and perceived helplessness. Finally, there is debate as to whether avoidant mechanisms reliably and validly characterize the phenomenology of PTSD. Perhaps social withdrawal and numbing of responsiveness ("emotional anesthesia") are not characteristic and only intrusive criteria (e.g., "flashbacks") should be used diagnostically.

In response to the call for prospective data to address these issues (2-5), we evaluated patients shortly after hospitalization for a burn injury and followed a representative sample for 1 year to determine the development of PTSD. We chose to study burn patients because the severity of the stressor can be objectively quantified and has a wide variance, because the distress associated with the trauma can be assessed shortly after the event, and because burn injury requiring hospitalization contains those elements presumed to be associated with PTSD (threat of disability or death; exposure to overwhelming stimuli; suddenness, unexpectedness, and unpreparedness; loss of loved ones and/or property; and direct involvement with the stressor) (6).

METHOD

Every adult patient admitted to our hospital's burn center was approached within the first week of hospi-

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talization. If the patient was able and willing to give informed consent, four subjective variables were measured: 1) emotional distress as measured by the Profile of Mood States (POMS) (7), which includes an assessment of state anxiety and helplessness, 2) perceived social support as measured by the Interpersonal Support Evaluation List (8), 3) intrusive thoughts during the past week about the burn injury as measured by the Impact of Event Scale (9), and 4) avoidant thoughts about the injury as measured by the Impact of Event Scale (9). The selection of these four subjective predictors of PTSD was based on a review of existing literature (2, 4–6, 10). Many patients are unable to write during the first few weeks following their injuries. For consistency in data collection, investigators read the questionnaires to all patients and marked their responses on the standardized instruments.

Objective severity of the stressor was assessed by using two measures: percent of total body surface area of the burn and percent of patients with facial disfigurement. Although not the primary focus of the study, we also estimated psychopathology before the burn by reviewing charts and interviewing available informants about any history of alcoholism, drug abuse, psychosis, and psychiatric hospitalization.

Patients were subsequently assessed at 2, 6, and 12 months after their burn injury. A clinical rating of PTSD was obtained by using the Structured Clinical Interview for DSM-III-R (SCID) (11). To examine the concurrent association between PTSD and psychological factors and to determine if these psychological factors predicted future PTSD, patients then completed the POMS and the Impact of Event Scale. The interviewers were blind to responses on these self-report measures. Patients geographically distant or otherwise unable or unwilling to attend follow-up assessments were clinically rated by a 30-minute telephone SCID interview and returned questionnaires by mail.

Logistic regression analyses were used to determine the extent to which baseline subjective and objective measures predicted PTSD at 2-month–12-month follow-up and to determine whether scores on the POMS and the Impact of Event Scale at 2-month and 6-month follow-up predicted PTSD at later assessments. Analyses of variance examined concurrent relationships between PTSD and the psychological measures (POMS and the Impact of Event Scale intrusive and avoidant thoughts). Since others (12) have reported a correspondence between PTSD and Impact of Event Scale cutoff scores (greater than 19 on both intrusive and avoidant thoughts about the injury), we examined the specificity and sensitivity of these cutoffs in our sample. Finally, we explored whether PTSD was predicted by sociodemographic variables and estimates of premorbid psychopathology.

RESULTS

Two-month follow-up data were obtained for 34 men and 17 women; 22 (43%) of these 51 patients were white,

16 (31%) were black, 11 (22%) were Hispanic, and two (4%) were "other"; 23 (45%) were married, 16 (31%) were single, and 12 (24%) were divorced or separated; 24 (47%) were skilled laborers, nine (18%) were homemakers, eight (16%) were unemployed, two (4%) were professionals, and eight (16%) did not provide data on their occupation. A history of alcoholism was documented in 12 (24%), other drug abuse in nine (18%), and psychosis or psychiatric hospitalization in eight (16%). Burns were due to flame injury ($N=38$, 75%), scalding ($N=11$, 22%), or chemical exposure ($N=2$, 4%).

Six-month follow-up data were available for 40 patients, and 12-month data were available for 31 patients.

An additional 78 patients were assessed within the first week of hospitalization but were lost to follow-up by 2 months after the injury. Two of these patients had died; 68 (89%) of the remaining 76 could not be located after discharge. (A change of address is a common consequence of burn injury and its associated physical, familial, and residential disruption.) Eight (11%) of the dropouts were located but refused to participate at the 2-month follow-up. At no follow-up assessment was attrition significantly related to age, sex, race, marital status, PTSD at a previous assessment, or hypothesized predictor variables (e.g., severity of distress or burn).

To assess the relative contributions of the independent variables (social support, body surface area burned, general distress, intrusive and avoidant thoughts, facial disfigurement) assessed at baseline in predicting PTSD, a forward stepwise logistic regression analyses was performed for each assessment time.

As shown in table 1, patients with smaller burns were more likely to meet criteria for PTSD at the 2-month assessment. PTSD at this assessment was also predicted by less perceived emotional support (Interpersonal Support Evaluation List) and greater emotional distress (POMS). Regarding subjective variables, less perceived social support at baseline (mean=7.2 days, $SD=1.1$, after burn injury), the first variable selected for inclusion in the regression model, predicted acute PTSD at 2-month follow-up (mean=10.5 weeks, $SD=1.9$, later). According to model chi-square (table 1), this variable made a significant improvement over the constant in predicting PTSD in this group of patients. Severity of emotional distress at baseline contributed to the prediction of acute PTSD (table 1). The severity of intrusive or avoidant thoughts during the first week of hospitalization did not predict acute PTSD. Regarding objective variables, the presence of facial disfigurement did not predict PTSD. Eleven (22.4%) of the 18 patients with PTSD at 2 months and 16 (30.6%) of the 33 patients without PTSD at 2 months had facial disfigurement at baseline. More extensive burn injury was also not associated with the development of PTSD. However, patients with smaller burns were significantly more likely to meet criteria for acute PTSD (table 1).

In the final model, the goodness-of-fit chi-square of 40.8 ($df=43$, $p=0.6$) had a high probability of occurrence; i.e., the null hypothesis that the model's predictions differ from the observed data was not confirmed.

TABLE 1. Physical and Psychological Predictors of PTSD 2 Months After Burn Injury

Variable at Baseline	Patients With PTSD at 2 Months (N=18)		Patients Without PTSD at 2 Months (N=33)		ANOVA		Logistic Regression		
	Mean	SD	Mean	SD	F (df=1, 49)	p	χ^2 Improvement (df=1)	p	β
Burned area (%)	13.1	9.0	21.8	1.6	7.6	<0.001	5.0	<0.05	-0.09
Scores on psychological measures at baseline									
Interpersonal Support Evaluation List	26.7	8.0	32.4	6.5	6.7	<0.01	6.4	<0.01	-0.10
POMS	8.2	5.7	3.8	4.6	8.5	<0.001	3.9	<0.05	0.17
Impact of Event Scale									
Intrusive thoughts	14.4	10.4	12.8	10.4	—		—		—
Avoidant thoughts	13.3	10.5	10.6	10.4	—		—		—

TABLE 2. Psychological Predictors of PTSD 6 Months After Burn Injury

Variable at 2 Months	Patients With PTSD at 6 Months (N=16)		Patients Without PTSD at 6 Months (N=24)		ANOVA		Logistic Regression		
	Mean	SD	Mean	SD	F (df=1, 38)	p	χ^2 Improvement (df=1)	p	β
POMS	8.1	4.7	2.9	4.9	8.8	<0.01	8.3	<0.01	0.11
Impact of Event Scale									
Intrusive thoughts	20.8	9.4	6.7	5.8	26.0	<0.01	8.7	<0.01	0.18
Avoidant thoughts	15.5	11.5	5.3	6.2	9.9	<0.01	—		—

TABLE 3. Psychological Predictors of PTSD 12 Months After Burn Injury

Variable at 6 Months	Patients With PTSD at 12 Months (N=14)		Patients Without PTSD at 12 Months (N=17)		ANOVA		Logistic Regression		
	Mean	SD	Mean	SD	F (df=1, 29)	p	χ^2 Improvement (df=1)	p	β
POMS	12.1	9.5	2.4	3.9	14.5	<0.001	9.2	<0.01	0.18
Impact of Event Scale									
Intrusive thoughts	22.1	12.3	8.1	10.0	13.9	<0.001	—		—
Avoidant thoughts	16.4	12.3	2.9	3.8	18.4	<0.001	3.3	<0.05	0.12

Thus, a regression model that predicts PTSD on the basis of social support, body surface area burned, and general emotional distress is a good predictive model.

In addition to predicting acute PTSD, social support was also a significant predictor of chronic PTSD at both 6 months (mean=26.5 weeks, SD=3.4) and 12 months after injury (mean=54.7 weeks, SD=3.4). Social support yielded a model chi-square of 4.9 (df=1, $p<0.03$) at 6 months and a model chi-square of 5.0 (df=1, $p<0.03$) at 12 months. None of the other hypothesized variables at baseline predicted PTSD at 6 or 12 months.

Tables 2 and 3 present the results of subsequent psychological assessments at 2 months and 6 months as predictors of PTSD. Severity of emotional distress at the previous follow-up appointment predicted the presence of PTSD at the next assessment. Severity of intrusive thoughts at 2 months predicted chronic PTSD at 6 months (table 2), and severity of avoidant thoughts at 6 months predicted chronic PTSD at 12 months (table 3).

As indicated in table 4, severity of emotional distress and both intrusive and avoidant thoughts were significantly associated with concurrent PTSD at all three fol-

low-up assessments. The association between PTSD and both intrusive and avoidant thoughts about the injury on the Impact of Event Scale cutoff scores was generally high. The cutoff for intrusive thoughts about the burn injury on the Impact of Event Scale correctly identified 79%, 100%, and 83% of those with PTSD and 81%, 78%, and 61% without the diagnosis at 2-, 6-, and 12-month follow-up, respectively, and the cutoff for avoidant thoughts about the injury on the Impact of Event Scale correctly identified 78%, 89%, 100% with PTSD and 74%, 71%, and 61% without the diagnosis.

Exploratory analyses found no significant relationship between future PTSD and sex, age, race, marital status, or estimates of premorbid psychopathology. To our knowledge, no patient received psychiatric treatment for the emotional impact of the burn trauma.

DISCUSSION

By assessing burn patients during the first week of hospitalization and then following a representative

TABLE 4. Psychological Variables and Concurrent Development of PTSD at 2, 6, and 12 Months After Burn Injury

Variable	Patients With PTSD			Patients Without PTSD			ANOVA		
	N	Mean	SD	N	Mean	SD	F	df	p
At 2 months									
POMS	18	9.4	5.2	33	2.7	4.6	19.3	1, 42	0.0001
Impact of Event Scale									
Intrusive thoughts	18	21.5	10.0	33	8.5	7.6	24.7	1, 45	0.0000
Avoidant thoughts	18	17.9	9.9	33	5.5	6.8	25.4	1, 45	0.0000
At 6 months									
POMS	16	13.3	9.4	24	2.2	4.6	16.3	1, 33	0.0003
Impact of Event Scale									
Intrusive thoughts	16	24.7	10.5	24	5.1	5.2	57.6	1, 36	0.05
Avoidant thoughts	16	15.2	11.2	24	4.5	6.7	13.5	1, 36	0.0008
At 12 months									
POMS	14	9.8	11.4	17	0.1	3.6	10.2	1, 24	0.004
Impact of Event Scale									
Intrusive thoughts	14	19.0	12.8	17	3.2	7.1	16.6	1, 25	0.0004
Avoidant thoughts	14	13.7	13.5	17	3.4	6.3	6.8	1, 25	0.001

sample for 1 year, we were able to examine what role subjective and objective factors play in the development of PTSD. We found that less perceived social support shortly following the trauma predicted PTSD at all three follow-up assessments, whereas more severe injury did not predict PTSD. Indeed, patients with smaller burns were more likely to meet criteria for acute PTSD.

One must be cautious in generalizing the results from a single study, particularly one in which all patients had experienced the considerable stressor of a burn injury. Nonetheless, this report does provide data for the long-standing debate about whether the development of PTSD is relatively more dependent on subjective factors than on the severity of the stressor. Our data lend support to the view that the individual's psychological state immediately following the event is more predictive of outcome than the degree of trauma (2, 13). These findings are pertinent to the deliberation over the inclusion of a subjective component for the stressor criterion in *DSM-IV*. The addition of subjective experience would include in the diagnosis those who may experience less severe stressors as overwhelming in the context of limited social support and its associated helplessness.

In regard to other suggested changes in the diagnostic criteria for PTSD, our data would support maintaining avoidant phenomenology. Like intrusive thoughts, endorsements of avoidant thoughts about the injury on the Impact of Event Scale were significantly associated with PTSD at each assessment.

Our findings may also be helpful in regard to clinical care, alerting clinicians about the high frequency of PTSD in burn patients and the emotional distress related to this disorder as measured by the POMS. At least a third of the patients we followed developed PTSD during the first year after the burn injury. Although patients who could not be located did not differ significantly from those who were followed on any variable measured at baseline, the rate of attrition precludes determining the prevalence of PTSD in this population. We doubt, however, that our reported high

rates are inflated. On the contrary, in the light of the association between less social support and future PTSD, we suspect that the prevalence of PTSD may be even higher among those who experienced a change of address as a result of residential fire and familial loss or disruption.

We were surprised that none of our patients reported seeking treatment for the residual emotional impact of their burn injuries. Possibly, the socioeconomic status of our sample made psychiatric treatment less accessible or affordable, but another possibility is that the avoidant ("numbing") mechanisms associated with PTSD impeded patients from seeking help or spontaneously describing their psychological symptoms to clinicians and others. Since we found that the severity of intrusive and avoidant thoughts after discharge was not only associated with concurrent PTSD but also helped predict future PTSD, those who provide follow-up surgical care and physical rehabilitation might consider administering the Impact of Event Scale at outpatient appointments. This rapidly scored self-report instrument requires less than 5 minutes to complete and could help guide early detection of current or future PTSD for further evaluation and psychiatric referral. Among our sample, the designated cutoff scores had adequate sensitivity and specificity for a screening measure.

More problematic is the prediction of PTSD during hospitalization while the patient is still in the throes of acute trauma and its treatment. Although counterintuitive, our findings would suggest that clinicians not use severity of the injury as a predictor. Similarly, severity of intrusive and avoidant thoughts during the first week after the injury was not associated with the development of PTSD, suggesting that such mental processes immediately after a severe trauma may be normal and, consistent with a modification in *DSM-III-R*, should be defined as pathological only if they persist. On the other hand, since we found that lower scores on the Interpersonal Support Evaluation List predicted PTSD throughout the first year, perhaps early supportive psychother-

apy should be targeted toward those burn patients who feel more socially isolated.

A limitation of this study was the absence of standardized assessment of psychopathology before the trauma. Although the estimated rates of previous alcoholism, drug abuse, psychosis, and psychiatric hospitalization suggest greater psychopathology in our sample than in community samples (14), this history did not predict PTSD, and most patients (56%) did not have an available history of these psychiatric disorders before their burns, supporting the findings of others that PTSD can occur in previously "normal" individuals (1, 2, 10). Despite this limitation, the prompt evaluation soon after the trauma, the quantifiable measures of both objective and subjective variables, and the prospective design have advantages over most other studies in examining variables that help predict, mediate, and define PTSD.

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Effectiveness of a Meditation-Based Stress Reduction Program in the Treatment of Anxiety Disorders

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Objective: This study was designed to determine the effectiveness of a group stress reduction program based on mindfulness meditation for patients with anxiety disorders. **Method:** The 22 study participants were screened with a structured clinical interview and found to meet the DSM-III-R criteria for generalized anxiety disorder or panic disorder with or without agoraphobia. Assessments, including self-ratings and therapists' ratings, were obtained weekly before and during the meditation-based stress reduction and relaxation program and monthly during the 3-month follow-up period. **Results:** Repeated measures analyses of variance documented significant reductions in anxiety and depression scores after treatment for 20 of the subjects—changes that were maintained at follow-up. The number of subjects experiencing panic symptoms was also substantially reduced. A comparison of the study subjects with a group of nonstudy participants in the program who met the initial screening criteria for entry into the study showed that both groups achieved similar reductions in anxiety scores on the SCL-90-R and on the Medical Symptom Checklist, suggesting generalizability of the study findings. **Conclusions:** A group mindfulness meditation training program can effectively reduce symptoms of anxiety and panic and can help maintain these reductions in patients with generalized anxiety disorder, panic disorder, or panic disorder with agoraphobia.

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Self-regulatory behavioral strategies, used alone or as adjuncts to other behavioral or medication regimens, may offer a unique approach to treating anxiety disorders. Three major self-regulatory strategies—meditation, relaxation, and biofeedback—are currently used in clinical practice for the treatment of anxiety. Research suggests that all three play a role in reducing both physiological and psychological components of

anxiety in normal populations and that the latter two techniques are effective in anxious populations, although with variable efficacy (1–6).

The research on meditation techniques has been largely limited to nonpsychiatric populations (7). To our knowledge, there are no studies of the effectiveness of meditation for patients with anxiety disorders as delineated by DSM-III or DSM-III-R criteria (8). Two controlled studies (9, 10) used meditation for patients with anxiety neurosis as defined by DSM-II criteria, but both lacked standardized diagnostic procedures. There was one uncontrolled study of patients diagnosed as having anxiety neurosis (11). None of these studies used a structured clinical interview for diagnosis. All of them investigated variants of one particular type of meditation, namely, transcendental meditation, in which the practitioner focuses on a mantra—a word or phrase repeated silently to achieve a meditative state.

In general, these studies suggested that transcendental meditation may be as effective as other behavioral techniques, such as biofeedback or relaxation, in the treatment of anxiety. Another uncontrolled study (12) investigated mindfulness meditation as an adjunct to psychotherapy for patients with a wide range of psychiatric disorders, excluding schizophrenia and other psy-

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choses. In that study, Kutz et al. found that according to both the patients' self-assessments and the therapists' assessments, there was moderate to marked improvement in a variety of psychological symptoms, including anxiety, from before to after treatment.

The lack of diagnostic assessment according to standardized diagnostic criteria in previous studies and the widespread practice of studying nonclinical populations (e.g., college students) limit the applicability of research findings regarding the clinical effectiveness of meditation. Moreover, the majority of the studies of the effects of meditation on anxiety have relied solely on measures of state-trait anxiety to determine outcome. Such measures do not adequately assess the presence of panic attacks or avoidance behavior and may fail to capture the complexity of clinically significant anxiety symptoms.

The present pilot study was devised to address some of the shortcomings of previous research that investigated the relation between meditation training and anxiety reduction. The study was conducted in conjunction with a well-established outpatient program for stress reduction and relaxation that involves intensive training in mindfulness meditation (13, 14), with emphasis on its practical applications in coping with stress and in enhancing adaptive health behaviors. Like other forms of meditation such as transcendental meditation, mindfulness meditation helps practitioners to cultivate greater concentration and relaxation (15). It differs specifically from transcendental meditation by training practitioners to attend to a wide range of changing objects of attention while maintaining moment-to-moment awareness (mindfulness), rather than restricting one's focus to a single object such as a mantra (16) (see the Method section for an operational definition). The choice of mindfulness as the primary meditative approach was due to its immediate applicability to a great variety of present-moment experiences. This orientation lends a quality of "ordinariness" to the intervention that makes it more acceptable and accessible to a wide range of people with different life stressors and different medical disorders (17).

The stress reduction and relaxation program serves a broad spectrum of patients with both physical and psychological disturbances (18). Previous studies have shown that participation in the program results in reductions in both physical and psychological symptoms of patients in many diagnostic categories. Chronic pain patients participating in the program reported markedly reduced levels of state anxiety (as measured with the Symptom Checklist-90-Revised) during the intervention period—levels that were maintained over a 4-year follow-up period (17, 19, 20). Similar changes were reported over a 2-year follow-up period by patients with stress-related medical disorders (Kabat-Zinn, unpublished manuscript).

The specific objectives of the present investigation were 1) to conduct a prospective outcome study, with a repeated measures design, to test the efficacy of treating patients diagnosed with anxiety disorders according to

DSM-III-R criteria in a well-established, meditation-based outpatient stress reduction program and 2) to examine whether variables at intake were predictive of outcome at follow-up.

METHOD

Potential subjects were selected from among all patients referred to the stress reduction and relaxation program in two consecutive cycles (spring and fall of 1988). The Symptom Checklist-90-Revised (SCL-90-R) (21) and the Medical Symptom Checklist (17) were administered to all patients referred to the program, as part of the intake evaluation. Those who scored above the 70th percentile on the anxiety subscale of the SCL-90-R and reported more than 10 anxiety-related symptoms (out of 37 possible symptoms) on the Medical Symptom Checklist were invited to take part in a formal screening interview to assess their appropriateness for inclusion in the study. A referral diagnosis of panic attacks or anxiety also qualified an individual to be invited to participate in the screening procedure for the study. Patients who met the study criteria and who agreed to participate were then interviewed by either a psychologist or a psychiatrist trained in administering the Structured Clinical Interview for *DSM-III-R* (SCID) (22). Diagnoses were determined after review of the SCID data by the two psychologists (J.K. and L.P.) and two psychiatrists (A.O.M. and L.G.P.) who conducted the individual screening evaluations. Only the patients who met the formal diagnostic criteria for generalized anxiety disorder or panic disorder with or without agoraphobia were included in the study. Individuals were excluded if they had other primary psychiatric diagnoses, any disorder with psychotic symptoms, any endocrine disorder, or significant current alcohol or substance abuse. Because of the small sample size and the pilot nature of the study, patients taking anxiolytic or other medications ($N=12$) were not excluded. Medication type and usage were assessed for all patients during the study.

In the two cycles of the program from which patients were recruited for this study, 192 (60%) of 321 patients satisfied the initial screening criteria of the SCL-90-R and the Medical Symptom Checklist. However, for logistical reasons and because this was a pilot study, only 44 patients were invited to undergo further screening, of whom 32 completed the evaluation. Of these, 24 met the *DSM-III-R* criteria for generalized anxiety disorder or panic disorder with or without agoraphobia according to the SCID. Of the eight excluded patients, four had other primary psychiatric diagnoses and four had no psychiatric disorder. Two of the 24 subjects did not complete the program and were not included in the analysis of outcome. Both of these individuals had psychiatric diagnoses of generalized anxiety disorder.

Because of the exploratory nature of the study, we used a repeated measures design with patients serving as their own controls on multiple pretreatment and post-

treatment measures. In addition, study participants were compared on the SCL-90-R and Medical Symptom Checklist with other patients who met the initial screening criteria and were enrolled in the stress reduction and relaxation program during the same time period but who were not invited to take part in the study. This second group of patients (termed "nonstudy participants") received the same meditation intervention but did not undergo screening or the weekly assessments that the study subjects underwent.

Subjects who met the diagnostic criteria and agreed to participate in the study were evaluated with both self-rating scales and ratings of trained interviewers. Data on the following measures were gathered by telephone interview at weekly intervals from the time of recruitment through the end of treatment and at monthly intervals for 3 months after treatment: the Beck Anxiety Inventory (used by special permission of Jeffrey Sugerman, Ph.D., Psychological Corp., personal communication), the Beck Depression Inventory (23), and ratings of the frequency and severity of panic attacks. The length of time between recruitment and the start of treatment in which data were collected varied according to when subjects were recruited into the study relative to the beginning of the program (range=1-8 weeks).

In addition to these assessments, a more extensive assessment battery was administered four times: at recruitment into the study, at the start of the program (pretreatment), at completion of the program (posttreatment), and at 3-month follow-up. This battery consisted of the Hamilton Rating Scale for Anxiety (24) (as modified by DiNardo and Barlow [25] to include a separate rating scale for symptoms present during panic attacks, yielding the Hamilton panic score), the Hamilton Rating Scale for Depression (26), the Fear Survey Schedule (27), and the Mobility Inventory for Agoraphobia (28). At recruitment patients were also asked to rate on a 5-point scale their expectancy of improvement due to the treatment. A compliance questionnaire was administered at the end of treatment and at follow-up. Eight subjects entered the study so close to the beginning of the treatment intervention that only pretreatment, posttreatment, and follow-up measures were obtained.

The Hamilton anxiety and depression rating scales were administered at recruitment by the same clinicians who administered the SCID. Subsequent Hamilton assessments were administered to all subjects by one trained interviewer. To minimize bias in data collection related to expectancy of change, scoring was done after all data were collected.

The stress reduction and relaxation program is a highly structured training program in mindfulness meditation and its applications, described in detail elsewhere (14, 17-20). It takes the form of an 8-week-long course in which participants attend weekly 2-hour classes and, in addition, a 7.5-hour intensive and mostly silent "meditation retreat" session in the sixth week. During each 8-week cycle, five separate but par-

allel classes are offered. Each is led by one instructor who stays with that group for the duration of the course. Each class has approximately 30 participants with a wide range of medical and psychological disorders. During classes and for homework, participants practice a range of different formal and informal meditation techniques (14, 17). These experiences are discussed weekly in the classes. The 22 subjects in this study were distributed among five of the 10 classes held during that period. The exposure of these subjects differed from that of the remainder of the program participants only in their involvement in the additional assessment protocol required for the study. Four program instructors conducted classes in this study. The instructors did not know which patients were in the study, nor did they know the patients' DSM-III-R diagnoses.

We used repeated measures analysis of variance (ANOVA) to compare the recruitment, pretreatment, posttreatment, and 3-month follow-up scores of the subjects for whom all data points were available, with computation of appropriate contrasts. Matched *t* tests were used to calculate intervention effects between the pretreatment and posttreatment assessments for the entire sample. Intergroup comparisons of compliance and expectancy measures were done with standard *t* tests. Variables expected to predict outcome were studied with ANOVA. We plotted the weekly scores of all subjects to examine the course of change, but formal single-subject analyses are not included in this report because of the consistency and strength of the group effects. In addition, after accounting for pretreatment scores with the regression technique described by Cohen and Cohen (29), we compared posttreatment scores of the subjects receiving medication with those of the subjects taking no medication. Finally, we used *t* tests to compare the study participants and nonstudy participants in the program on pretreatment and posttreatment SCL-90-R scores, Medical Symptom Checklist scores, and change scores.

RESULTS

Of the 22 study participants who completed the program, 10 had panic disorder with agoraphobia, four had panic disorder without agoraphobia, and eight had generalized anxiety disorder as the primary psychiatric diagnosis. Seventeen subjects had more than one psychiatric diagnosis; 14 had other anxiety disorders and eight had diagnoses of major depressive episode (six concurrent). The average duration of their anxiety disorders was 6.5 years (range=3 months to 28 years). Eleven patients were taking medication for their anxiety disorders at intake, and 11 were taking no medication for anxiety.

The subjects' ages ranged from 26 to 64 years, with an average of 38 years. There were five men and 17 women. Eighteen of the subjects were married, two were single, and one was separated (data on one subject were missing).

The recruitment and pretreatment scores on the Ham-

TABLE 1. Scores on Outcome Measures Over Time of Patients With Anxiety Disorders in a Study of a Meditation-Based Stress Reduction Program

Measure	N	Initial Recruitment		Pretreatment		Posttreatment		3-Month Follow-Up		Repeated Measures ANOVA		
		Mean	SD	Mean	SD	Mean	SD	Mean	SD	F	df	p
Hamilton Rating Scale for Anxiety	14	30.36	8.53	26.93	11.13	17.86	9.18	15.86	8.65	21.1	3, 39	<0.001 ^a
Hamilton Rating Scale for Depression	14	33.07	7.98	31.07	8.43	23.71	5.59	25.14	7.01	8.87	3, 39	<0.001 ^a
Beck Anxiety Inventory	15	24.13	13.49	20.53	13.24	9.00	9.14	7.93	7.29	15.36	3, 42	<0.001 ^a
Beck Depression Inventory	15	18.87	10.37	16.47	10.97	10.00	9.58	7.53	8.77	9.96	3, 42	<0.001 ^{a,b}
Fear Survey Schedule	11	118.73	41.31	93.55	34.09	78.46	44.28	66.82	38.68	9.79	3, 30	<0.001 ^{c,d}
Mobility Inventory for Agoraphobia												
Accompanied	10	45.80	16.22	41.30	16.81	36.40	12.02	36.70	13.52	4.05	3, 27	<0.05 ^e
Unaccompanied	10	61.80	24.40	53.50	24.09	45.50	17.19	46.20	18.87	6.62	3, 27	<0.01 ^{c,e}

^aSignificant change from pretreatment to posttreatment ($p < 0.01$).^bTrend for significant change from posttreatment to follow-up ($p < 0.10$).^cSignificant change from recruitment to pretreatment ($p < 0.05$).^dSignificant change from posttreatment to follow-up ($p < 0.05$).^eTrend for significant change from pretreatment to posttreatment ($p < 0.10$).

ilton Rating Scale for Anxiety, the Hamilton Rating Scale for Depression, the Beck Anxiety Inventory, the Beck Depression Inventory, the Fear Survey Schedule, and the Mobility Inventory for Agoraphobia of the subjects with complete data at the four primary assessment points are shown in table 1. They were in the moderate to severe range on both the Beck and the Hamilton anxiety scales and in the mild to moderate range on the Beck and Hamilton depression scales.

At recruitment, nine individuals reported one or more panic attacks in the previous week (range=1–3), with a mean Hamilton panic score of 26.11 (SD=11.25, range=6–40). At pretreatment assessment, 13 individuals reported at least one panic attack in the previous week (range=1–2), with a mean Hamilton panic score of 24.46 (SD=8.71, range=11–34). At pretreatment the mean SCL-90-R general severity index score of the 22 subjects was 1.10 (SD=0.70, range=0–3) and the mean SCL-90-R anxiety score was 1.61 (SD=1.05, range=0–3).

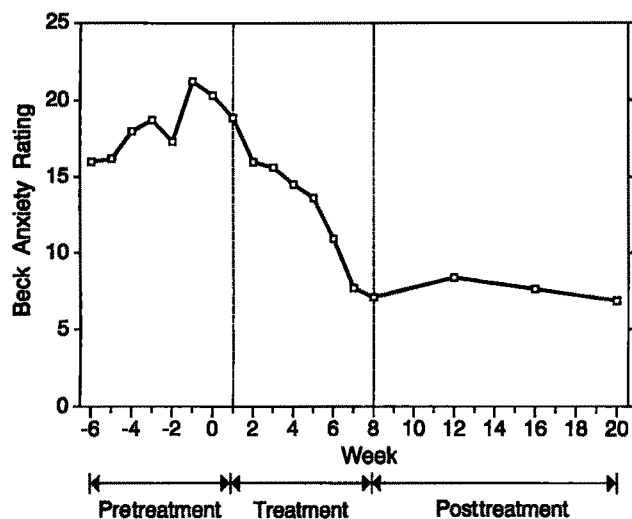
Repeated measures ANOVA indicated that among subjects for whom scores at all four primary assessment points were available, the Hamilton and Beck anxiety and depression scale scores showed small, statistically nonsignificant reductions from baseline to pretreatment, highly significant decreases over the course of the intervention (pretreatment to posttreatment), and maintenance of these changes from posttreatment to follow-up (table 1). Comparisons with matched *t* tests at pretreatment and posttreatment time points for all subjects, not just those with complete data at all time points, showed comparable results, with mean pretreatment and posttreatment scores, respectively, of 25.86 (SD=10.56) and 17.10 (SD=9.31) on the Hamilton anxiety scale ($t=5.18$, $df=20$, $p < 0.001$) and 30.85 (SD=8.81) and 23.85 (SD=6.65) on the Hamilton depression scale ($t=4.88$, $df=19$, $p < 0.001$). Mean pretreatment and posttreatment scores, respectively, were 20.32 (SD=12.05) and 7.09 (SD=8.20) on the Beck Anxiety Inventory ($t=6.14$, $df=21$, $p < 0.001$) and 16.18 (SD=10.33) and 8.18 (SD=8.53) on the Beck Depression Inventory ($t=4.65$, $df=21$, $p < 0.001$). These represented mean reductions of 34%, 23%, 65%, and 49%, respectively,

on the four scales. Twenty of the 22 subjects showed marked improvement in scores on the Beck and Hamilton anxiety and depression scales.

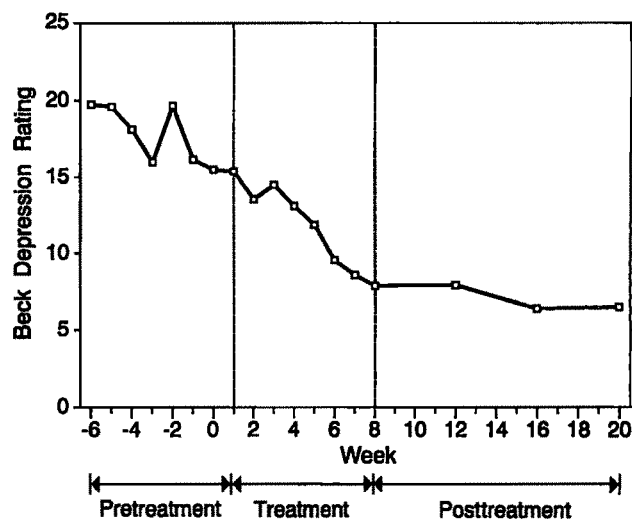
The means of the subjects' weekly ratings of anxiety and depression on the respective Beck scales are presented in figures 1 and 2. These show elevated levels before treatment, a significant decline during treatment to a relatively low level by the end of treatment, and maintenance of the lower posttreatment level over 3 months of follow-up. Scores for "accompanied" on the Mobility Inventory for Agoraphobia showed a similar pattern of improvement. However, scores for "unaccompanied" on that inventory and scores on the Fear Survey Schedule improved as much from recruitment to pretreatment assessment as from pretreatment to posttreatment assessment (table 1).

Of the 13 patients who reported at least one panic attack in the preceding week at pretreatment assessment, five reported one panic attack in the previous week at posttreatment assessment (mean Hamilton panic score=22.0, SD=8.40, range=13–34). At 3-month follow-up, three of the original 13 patients reported one attack in the previous week (mean Hamilton panic score=18.0, SD=6.24, range=11–23). This was a statistically significant decrease in the number of individuals reporting panic attacks from pretreatment to posttreatment to follow-up assessment (Cochran's $Q=14.60$, $df=2$, $p < 0.001$, $N=20$). Within this group, the individuals whose primary psychiatric diagnosis was panic disorder with or without agoraphobia also showed a statistically significant linear decrease from pretreatment to posttreatment to follow-up (Cochran's $Q=12.67$, $df=2$, $p < 0.005$, $N=13$).

In both groups there was a significant decline in Hamilton panic scores between pretreatment and posttreatment assessments. For the subjects who reported at least one panic attack at pretreatment assessment ($N=13$), the mean pretreatment Hamilton panic score was 24.46 (SD=8.71) and the mean posttreatment Hamilton panic score was 8.46 (SD=12.15) ($t=4.75$, $df=12$, $p < 0.001$). For the panic disorder subset ($N=11$), the mean pretreatment Hamilton panic score was 24.64

FIGURE 1. Mean Beck Anxiety Inventory Ratings Before, During, and After Treatment of Patients in a Meditation-Based Stress Reduction Program^a

^aThe numbers of subjects for successive assessments were as follows: pretreatment, 4, 5, 7, 11, 12, 16, 21; treatment, 20, 22, 22, 21, 22, 21, 21, 19; posttreatment, 21, 19, 21.

FIGURE 2. Mean Beck Depression Inventory Ratings Before, During, and After Treatment of Patients in a Meditation-Based Stress Reduction Program^a

^aThe numbers of subjects for successive assessments were as follows: pretreatment, 4, 5, 7, 11, 12, 17, 21; treatment, 20, 22, 21, 21, 22, 21, 22, 19; posttreatment, 21, 20, 21.

(SD=8.30) and the mean posttreatment Hamilton panic score was 8.36 (SD=12.68) ($t=4.07$, $df=10$, $p<0.005$). The mean number of panic attacks registered on the Hamilton anxiety scale and their severity also declined significantly between pretreatment and posttreatment assessments in both groups, and these declines were maintained at 3-month follow-up (data not shown).

The pretreatment and posttreatment scores of the subjects receiving psychotropic medication did not differ significantly from those of the subjects not receiving medication during the study. Twelve patients were taking medication for anxiety before treatment and 13 after treatment; 11 were taking medication at follow-up. Two patients were able to decrease their use of medication between the posttreatment and follow-up assessments, and one increased the use of medication during the same period.

The pretreatment and posttreatment scores on the SCL-90-R and the Medical Symptom Checklist of the study participants in the stress reduction and relaxation program were compared with the scores on these scales of the nonstudy participants in the program who had met the initial screening criteria for the study to assess possible biasing effects from the more intense assessment protocol on the study participants. As can be seen in table 2, the mean pretreatment and posttreatment scores on the total Medical Symptom Checklist, the anxiety items of the Medical Symptom Checklist, the general severity index of the SCL-90-R, and the anxiety subscale of the SCL-90-R for the 22 subjects in the study were comparable to those of the nonstudy participants in the program. The two groups showed statistically significant and equivalent symptom reduction on these measures over the intervention period.

When changes from before to after treatment in anxiety scores and in the number of panic attacks were examined on an individual basis, 20 of the 22 study subjects showed marked improvement (only one patient still had a score over 20 on the Beck Anxiety Inventory after treatment), making it difficult to examine predictors of differential outcome. Consistent with this uniformity of response, no demographic or baseline variables were significantly predictive of outcome. Expectancy ratings also failed to serve as a meaningful predictor of outcome. Self-reported amount of practice (compliance) was also not significantly correlated with any outcome measure. Furthermore, there were no statistically significant differences in outcome between patients with generalized anxiety disorder and those with panic disorder with or without agoraphobia, nor was the diagnosis of major depressive episode associated with outcome.

Adherence to the meditation practices taught in the stress reduction and relaxation program was assessed at 3-month follow-up. In response to the question "Have you been keeping up practice of the stress reduction techniques?" 91% (20 of the 22 subjects) replied in the affirmative, with a relatively homogeneous distribution between single meditation techniques and combinations of methods. Eighty-four percent ($N=16$) of the 19 who responded to this item were practicing formally three or more times per week; 42% ($N=8$) were practicing for 45 minutes or more at a time, 16% ($N=3$) for between 30 and 45 minutes at a time, and 37% ($N=7$) for between 15 and 30 minutes at a time. Twenty-one subjects reported continued use of mindfulness of breathing (an informal mindfulness practice) in their daily lives, with 77% ($N=17$) using it "often" and 18% ($N=4$) using it "sometimes."

DISCUSSION

The rate of completion of the program among the study subjects was high (22 of 24 subjects, or 92%), consistent with previous studies of the stress reduction and relaxation program (18). Twenty of 22 subjects showed marked improvement in both anxiety and depression after the intervention. This improvement was maintained at 3-month follow-up. Improvement was observed both in patients' self-ratings (Beck anxiety and depression scales) and in interviewers' ratings (Hamilton anxiety and depression scales).

Of considerable importance is the statistically significant reduction from pretreatment assessment to post-treatment assessment in the number of subjects reporting one or more panic attacks, an improvement that was maintained at follow-up. There was a statistically nonsignificant tendency for the Hamilton panic scores to decrease between pretreatment and follow-up, suggesting that for the subjects who continued to have panic attacks during and after the intervention, the severity of those attacks declined.

Fear survey and mobility inventory scores also improved significantly, but these changes began during the pretreatment period, suggesting both an effect of the general expectancy of participation and an effect of the exposure to a therapeutic milieu during the evaluation visits.

The uniformly positive response to treatment among the subjects in this small study precluded a successful analysis of predictors of outcome. Compliance was also uniformly reported as moderate to high, indicative of the subjects' positive response to the intervention approach and the successful adoption of a range of new behaviors, including both formal and informal meditation practice.

A major strength of this study was the careful diagnostic assessment procedure we used to obtain *DSM-III-R* diagnoses. Previous studies investigated the use of meditation with normal populations or populations identified by using only nondiagnostic criteria. Such studies may therefore have included patients who would not have met the *DSM-III-R* criteria for generalized anxiety disorder or panic disorders. The results of this study, which focused specifically on patients with generalized anxiety disorder or panic with or without agoraphobia, suggest that mindfulness meditation used in a group format may be a useful treatment approach for these diagnostic groups.

It is also clear that the improvements in panic and anxiety which we observed cannot be attributed solely to participation in the study itself. This is established by the comparison showing that the subjects who participated in the study and the patients in the stress reduction program who met the screening criteria but were not subjected to the intensive research protocol achieved similar reductions in anxiety scores on the SCL-90-R and the Medical Symptom Checklist. This comparison also demonstrates that the results obtained with the study subjects are very likely generalizable to

TABLE 2. Pretreatment and Posttreatment Scores of Patients With Anxiety Disorders in a Study of a Meditation-Based Stress Reduction Program Compared With Scores of Nonstudy Participants in the Program Who Met Initial Screening Criteria for the Study^a

Measure	Study Participants in Program			Nonstudy Participants in Program		
	N	Mean	SD	N	Mean	SD
Medical Symptom Checklist	21			99		
Total score						
Pretreatment		32.05	13.33		30.97	11.55
Posttreatment		23.10	17.75		19.59	12.66
Anxiety score ^b						
Pretreatment		16.95	0.51		15.96	4.67
Posttreatment		11.10	8.50		10.17	5.53
SCL-90-R	20			97		
General severity index score						
Pretreatment		1.08	0.73		1.03	0.56
Posttreatment		0.60	0.54		0.62	0.45
Anxiety subscale score						
Pretreatment		1.56	1.08		1.27	0.79
Posttreatment		0.69	0.68		0.70	0.62

^aAll within-group differences between pretreatment and posttreatment scores were significant ($p < 0.05$) in the two-tailed paired *t* tests. None of the pretreatment scores differed significantly between study participants and nonstudy participants in the unpaired *t* tests, except on the anxiety subscale of the SCL-90-R, for which $p = 0.05$.

^bMean number of symptoms out of the 37 identified as characteristic of patients with anxiety disorders.

the much larger group of patients who met the initial criteria for the study.

The strong reductions in panic symptoms and frequency of panic attacks observed in this study are consistent with the cognitive model of panic (30) and with clinical outcomes from studies of panic disorder in which well-established cognitive (31) and cognitive-behavioral (32) intervention approaches were used. The meditative approach used in the stress reduction and relaxation program shares some attributes with both cognitive and behavioral therapeutic approaches used to treat anxiety and panic. It also differs structurally and theoretically from them in a number of noteworthy respects, as has been noted in a different context by others (33, 34).

In particular, the meditative, cognitive, and cognitive-behavioral approaches share an emphasis on noting sensations and thoughts without viewing them as catastrophic and the use of stress-inducing situations as cues to engage in new behaviors. They also have in common the use of homework assignments to reinforce what was learned in the group sessions. However, the stress reduction and relaxation program differs from cognitive and cognitive-behavioral models in the following important respects.

1. Emphasis is not placed on distinguishing thoughts as positive, negative, or faulty, as in cognitive therapy. Rather, the emphasis is on identifying thoughts as "just" thoughts and acknowledging the potential inaccuracy and limits of all thought, not just thoughts that produce anxiety. This attitude is cultivated in the peri-

ods of formal meditation practice, as well as in informal mindfulness practiced in the course of daily activity.

2. The formal meditation is taught as a daily discipline to be practiced regularly, independent of one's state of anxiety. The emphasis is on meditation as a way of being, as a way of living one's life, and as a way to develop alternative "generic" strategies for coping with stress and pain, rather than as a technique for coping with a specific problem such as panic.

3. The intervention takes place in a nonpsychiatric medical setting with a heterogeneous group of patients who have a wide range of medical and psychological problems. This is a significant departure from the model of cognitive-behavioral therapy, which is typically provided to individuals or groups of patients with a single disorder. Moreover, the focus of the intervention is on the meditation practice itself rather than on a specific disorder or diagnosis or constellation of symptoms.

4. Unlike Barlow's cognitive-behavioral approach, in which subjects are systematically exposed through specific induction exercises to feared internal sensations associated with panic, such as cardiovascular symptoms, hyperventilation, dizziness, and chest muscle tightness (35), there is no attempt at systematic desensitization through the induction of symptoms of any kind during the stress reduction and relaxation program. Although stressful or anxiety-related symptoms are not intentionally evoked, when these experiences arise, either during formal meditation or in the course of daily living, patients are encouraged to see them as opportunities to engage in mindful coping strategies as an alternative to more habitual patterns of emotional reactivity. In this respect, the program utilizes a cognitive restructuring that overlaps with other cognitive and cognitive-behavioral approaches.

5. The observational skills cultivated through mindfulness training differ substantially from those developed by behavioral monitoring techniques. Participants in the program are trained initially to develop concentration (one-pointed attention) through systematic and continued focusing on a restricted field of observation such as breathing or proprioception. Concentration lends stability to one's capacity to observe fearful thoughts and feelings in a nonreactive way. Coupled with mindfulness, concentration gives rise to a nondiscursive, nonanalytical, direct experiencing of the object of attention. This is in contrast to the external data gathering involved in behavioral analysis of antecedents and consequences.

Patients who are able to identify anxious thoughts as *thoughts*, rather than as "reality," report that this alone helps reduce their anxiety and increases their ability to encounter anxiety-producing situations more effectively. The insight that one is not one's thoughts means that one has a potential range of responses to a given thought if one is able to identify it as such. This increased range of options is associated with a feeling of control. It might be hypothesized that this is a feature of a cognitive pathway explaining the clinical observations in this study.

With regard to treatment validation, it should be noted that the duration of meditation practice in the weekly classes becomes incrementally longer over the course of the intervention. By the eighth week, most patients sit in silence in class, with little overt movement for periods of up to 45 minutes. This is a profound behavior change for most patients with panic disorder or anxiety. Such extended periods of stillness serve as an observable behavioral indicator of an individual's increasing ability to concentrate and achieve a degree of calmness over the intervention period. The all-day silent intensive session in the sixth week of the program, involving over 150 patients in one large room, is also an empirical indicator of the development of new behavior. It can be a substantial challenge for patients with panic disorder to sit still for long periods of time, attempting to observe anxious thoughts and impulses as they arise and working with them mindfully rather than succumbing to impulses of reactivity and panic.

A salient limitation of this pilot study is that it did not have a randomly selected comparison group. It also lacked a control for concomitant treatment. However, the group of patients receiving medication showed symptom reduction equivalent to that of the group not receiving any medication, a finding which suggests that the mindfulness approach may be equally useful for patients who receive pharmacotherapy and those who do not. As in treatment studies comparing imipramine and alprazolam (36, 37) and a study of nonpharmacological therapies (6), patients with generalized anxiety disorder and patients with panic disorder responded equally well to the program intervention. However, the number of patients in these two diagnostic categories was small, and a larger, randomized study would be required to determine whether the stress reduction and relaxation program is equally effective in each case or in the case of patients who are receiving pharmacotherapy compared with those who are not. A larger randomized study would also be valuable for comparing the mindfulness-based intervention with other cognitive and cognitive-behavioral therapies.

We observed parallel changes in anxiety and depression scale scores after the meditation program that were similar to those noted by Borkovec et al. (5). However, the presence of comorbid depression in eight subjects in our study was not associated with a statistically significant difference in outcome, as was previously reported (38). This result could mean that the intervention was helpful in alleviating depressive as well as anxiety symptoms. Alternatively, it could have been an artifact of the small size of the study group.

In summary, this pilot study of the efficacy of training in mindfulness meditation in the context of a group stress reduction clinic for medical outpatients showed statistically and clinically significant reductions in symptoms of anxiety and depression in patients with the three core anxiety disorders (generalized anxiety disorder, panic disorder, and panic disorder with agoraphobia) diagnosed according to the *DSM-III-R* criteria. These changes appeared to be independent of par-

ticipation in the research protocol and were maintained at 3-month follow-up.

ADDENDUM

A recently completed long-term follow-up conducted with 18 of the 22 subjects in this study found that after 3 years, the 3-month follow-up levels of anxiety and depression reported here had been maintained.

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Brief Treatment of Emergency Room Patients With Panic Attacks

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Objective: Most research on treatment for panic disorder has involved chronic forms of the illness. To determine the efficacy of early intervention, the authors examined the effects of treatment for patients with panic attacks who were seen in the emergency room, which is the first point of contact with the health delivery system for many persons with panic attacks. **Method:** The subjects were 33 patients with panic attacks seen in two emergency rooms. The presence of panic attacks was confirmed with a modified version of the Structured Clinical Interview for DSM-III-R; approximately 40% of the patients met the DSM-III-R criteria for panic disorder with agoraphobia. The patients were randomly assigned to groups receiving reassurance (N=16) or exposure instruction (N=17). Scores on the Fear Questionnaire agoraphobia subscale, Mobility Inventory, and Beck Depression Inventory and the frequency of panic attacks were determined at baseline, 3 months, and 6 months. **Results:** The subjects who received exposure instruction significantly improved over the 6-month period on depression, avoidance, and panic frequency. The reassurance subjects did not improve on any measure and eventually reported more agoraphobic avoidance. **Conclusions:** These results suggest that early intervention with exposure instruction may reduce the long-term consequences of panic attacks. The exposure instruction was of value even though the subjects had relatively low levels of avoidance at the outset of the study.

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Panic disorder is common in the general population (1), and individuals with panic attacks are frequent users of health services (2). Although much has been written about pharmacological and behavioral treatments for panic-related disorders (3, 4), and there is evidence of a decline in the utilization of health care services by successfully treated agoraphobic patients (5), most of the available literature relates to the treatment of relatively chronic forms of panic disorder. For example, the average length of illness of patients studied in phase I of the Cross-National Collaborative Panic Study (6) was 8 years. Because the emergency room is the first point of contact with the health delivery system for many persons with panic attacks, we examined the effects of

treatment for emergency room patients with panic attacks to determine the efficacy of early intervention.

METHOD

Subjects

Forty patients (23 men, 17 women) in the emergency rooms of two large Toronto hospitals volunteered to undergo the initial assessment interview. Of these 40 patients, 33 (20 men, 13 women) agreed to random assignment to treatment and to follow-up. The age range of these subjects was 19-58 years (mean=31.5 years), and there were no significant differences in demographic variables between the two treatment groups. The Ontario Health Insurance Plan provides no-cost medical services, including emergency room visits, to all residents of Ontario, so access to emergency and ongoing medical care is affected little by financial status.

Procedure

Physicians working in the emergency room were aware of the nature of panic disorder and its somatic

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TABLE 1. Effect of Exposure Instruction or Reassurance on Symptoms of Emergency Room Patients With Panic Attacks

Variable	Exposure Instruction (N=17)		Reassurance (N=16)		ANOVA	
	Mean	SD	Mean	SD	F (df=1, 31)	p
Test scores						
Beck Depression Inventory						
Baseline	8.82	7.94	9.75	6.66	0.13	n.s.
Midpoint	4.06	3.77	8.88	5.41	8.89	0.006
Endpoint	4.06	4.10	9.56	5.27	11.30	0.002
Mobility Inventory						
Baseline	1.56	0.73	1.50	0.78	0.05	n.s.
Midpoint	1.31	0.50	1.62	0.82	1.77	n.s.
Endpoint	1.30	0.51	1.61	0.83	1.72	n.s.
Fear Questionnaire, agoraphobia subscale						
Baseline	4.35	6.34	4.13	5.72	0.01	n.s.
Midpoint	2.65	4.17	5.40	6.48	2.09	n.s.
Endpoint	2.53	4.16	5.47	6.37	2.44 ^a	n.s.
Panic attacks in previous week						
Baseline	2.53	3.34	2.50	3.52	0.00	n.s.
Midpoint	0.88	1.36	2.31	4.41	1.63	n.s.
Endpoint	0.76	1.52	3.38	5.71	3.30	0.08

^adf=1, 30.

presentation because of ongoing research on hyperventilation in the emergency room. Panic patients were seen by the attending emergency room physician, who excluded the presence of actual physical disease. These patients were then informed of the study by emergency room staff and, if they consented, were contacted within 24 hours by one of us (C.S.). The patients were seen before they left the emergency room or were interviewed within 2 days of their initial emergency room contacts.

At the first interview the patient was assessed with a modified version of the Structured Clinical Interview for DSM-III-R (7) to confirm the presence of panic attacks and rule out other psychiatric disorders. Approximately 40% of the patients met the DSM-III-R criteria for panic disorder with agoraphobia. In almost all cases the patients were just beginning to experience panic attacks and did not have long histories of panic. All subjects were informed of the voluntary nature of the study and signed consent statements.

Before the treatment sessions, phobic avoidance and fear were assessed with the agoraphobia subscale of the Fear Questionnaire (8) and the Mobility Inventory (9). Depressed mood was assessed with the Beck Depression Inventory (10), and panic attacks were assessed by a patient-therapist consensual agreement similar to the procedure used in the Cross-National Collaborative Panic Study (6). The patients completed the self-report measures and panic diaries at baseline, 3 months, and 6 months. One of us (C.S.) interviewed all subjects. This author was not blind to the treatment conditions, and to reduce expectation bias we used only self-report measures.

After the initial interview each subject was assigned, by predetermined randomization, to a reassurance group (N=16) or an exposure instruction group (N=17). Each subject was reassured that what he or she had

experienced was a panic attack and that there was no physical or psychiatric disorder. The exposure instruction group was given additional information beyond that given to the reassurance group. Each subject who received exposure instruction was told that the most effective way to reduce the fear was to confront the situation in which the attack had occurred. The subject was advised to return to this situation as soon as practicable after the interview and to wait there until the anxiety decreased. All sessions were individual, no treatment goals were set, and there was no ongoing contact with the initial interviewer. Each session lasted approximately 60 minutes. The self-report measures were mailed to the subjects a week before the 3-month and 6-month follow-up visits.

RESULTS

A 2x3 (Treatment by Time) mixed factorial multivariate analysis of variance was conducted for each of the dependent variables with Greenhouse-Geisser corrected degrees of freedom. There were significant Treatment by Time interactions on the agoraphobia subscale of the Fear Questionnaire ($F=9.40$, $df=1, 30$, $p<0.001$), on the Mobility Inventory ($F=8.64$, $df=1, 31$, $p<0.001$), and on the measure of panic frequency ($F=3.59$, $df=1, 31$, $p<0.04$). On the Beck Depression Inventory, the Treatment by Time interaction approached statistical significance ($F=3.04$, $df=1, 31$, $p=0.06$).

The results of the post hoc analyses of the scores of the two groups at baseline, 3 months, and 6 months are presented in table 1. There were no significant differences between the two groups at baseline on any measure. The level of phobic avoidance, as measured by the Fear Questionnaire agoraphobia subscale and the Mobility Inventory, was somewhat low at baseline for both

groups. This was not unexpected since the selection of subjects was based on the experience of panic attacks and not the diagnostic criteria for panic disorder or agoraphobia. The exposure instruction group scored significantly lower than the reassurance group on the Beck Depression Inventory at midpoint and endpoint. The frequency of panic attacks in the previous week decreased from 2.53 to 0.76 in the exposure instruction group and increased from 2.50 to 3.38 in the reassurance group. The endpoint difference approached statistical significance.

The exposure and reassurance groups were each examined for changes in scores over time. The exposure instruction group significantly improved on all measures over time—Beck Depression Inventory: $F=7.78$, $df=1, 31$, $p<0.002$; Mobility Inventory: $F=8.56$, $df=1, 31$, $p<0.002$; Fear Questionnaire agoraphobia subscale: $F=6.65$, $df=1, 30$, $p<0.003$; panic frequency: $F=4.13$, $df=1, 31$, $p<0.03$). The reassurance group did not significantly improve on any measure over time. In fact, they became significantly more agoraphobic as shown by their scores on the Fear Questionnaire agoraphobia subscale ($F=3.18$, $df=1, 30$, $p<0.05$).

DISCUSSION

Little is known of the natural history of panic disorder with agoraphobia or the effects of early intervention. The results of this study, for a small group of patients, suggest that early intervention with exposure instructions in a setting that is often the first contact point for health care delivery may reduce the long-term consequences of panic attacks. It is noteworthy that exposure instructions were of value even though the standard measures of agoraphobia revealed relatively low levels of avoidance at the outset. The results also

suggest that reassurance is insufficient to reduce the catastrophic misinterpretation of panic symptoms. These patients became significantly more agoraphobic over the 6-month follow-up period, and this progression may represent the natural course of panic attacks and agoraphobia.

While the present results await replication, we suggest that all patients seeking treatment for panic attacks be given exposure instructions as part of their early assessment or treatment.

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Onset of Obsessive-Compulsive Disorder in Pregnancy

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Objective: Although the role of pregnancy and childbirth in postpartum psychosis and depression has been studied, the association between pregnancy and obsessive-compulsive disorder has not been specifically addressed. The authors evaluated the role of pregnancy in the onset of obsessive-compulsive disorder. **Method:** Female patients with obsessive-compulsive disorder (N=106) completed a questionnaire assessing age at onset of symptoms, marital status, number of children, age at each pregnancy, and life events associated with the onset of obsessive-compulsive disorder. **Results:** Of the 106 women, 42 were childless and 59 had at least one child each; five others were also childless but had had abortions (N=4) or a miscarriage (N=1). Of the 42 women without children, 12 (28.6%) had first experienced obsessive-compulsive symptoms between the ages of 13 and 15 years, but there were two peaks of onset for the women with children: ages 22–24 and 29–32 years. Of the 59 patients with children, 23 (39.0%) had experienced symptom onset during pregnancy; this was the first pregnancy for 12, the second pregnancy for eight, and the third pregnancy for three. Four of the five women who had had abortions or a miscarriage had experienced the onset or an exacerbation of obsessive-compulsive symptoms during pregnancy. **Conclusions:** The association between pregnancy and the onset of obsessive-compulsive symptoms in these female patients highlights the need for further research on psychological and biological factors associated with pregnancy and obsessive-compulsive disorder.

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The role of biological and psychological factors in the onset of psychiatric symptoms needs further exploration. In particular, the role of pregnancy in obsessive-compulsive disorder deserves empirical assessment. During interviews and treatment of over 500 patients with obsessive-compulsive disorder by two of us (F.N., J.A.Y.-T.), it was observed that the onset of obsessive-compulsive disorder for many women appeared to be during pregnancy.

A review of the literature indicated an abundance of works on the role of pregnancy and childbirth in postpartum psychosis (1–4) and depression (5–10) but only a handful of articles on the relationship between life events, in particular pregnancy, and onset of obsessive-compulsive disorder. Through information provided by psychiatrists, social workers, and self-report, Pollitt (11) found that pregnancy and childbirth were associ-

ated with the onset of obsessive-compulsive disorder in 11% of inpatients and outpatients with obsessive-compulsive disorder. The diagnoses of obsessional illness in the outpatients had been made by one private practitioner, and the inpatients had been diagnosed by many different practitioners, so the reliability of the diagnoses is questionable. Ingram (12), in reviewing detailed case records and personally interviewing and diagnosing hospital patients with obsessional states, noted that for 16.9% of the total patient group the onset had occurred in association with pregnancy, but Lo (13) reported such an association in only 5% of patients. In two case histories (5, 14) obsessive-compulsive symptoms were exacerbated either during pregnancy or during the puerperal period. In addition, the onset of obsessive-compulsive disorder has been associated with viewing or feeling guilty about having repeated abortions (15, 16). The authors of a recent report (17) mailed a questionnaire to 180 consecutively evaluated obsessive-compulsive disorder patients in their database, and 27 (69%) of the 39 female patients described a relationship between the onset or an exacerbation of obsessive-compulsive disorder and some aspect of pregnancy, birth, or care of their children. The wide range of percentages reported in the studies described may be accounted for by the different methods of data collection, the lack of uniform diagnostic criteria, and different patient populations with varying degrees of severity.

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TABLE 1. Ages at Onset of Obsessive-Compulsive Disorder and at Pregnancy for 106 Women With or Without Children

Age Variable (years)	With Children (N=59)	Without Children (N=42)	Abortion (N=4) ^a	Miscarriage (N=1) ^a
Age at study				
Mean	41	38	36	28
Range	20–78	24–63	29–56	28
Age at onset of obsessive-compulsive disorder				
Mean	25	23	20	28 ^b
Median	23	19	—	
Mode	22	14	20	
Age at pregnancy				
First pregnancy (N=59)				
Mean	26			
Mode	23			
Second pregnancy (N=37)				
Mean	29			
Mode	29			
Third pregnancy (N=15)				
Mean	31			
Mode	33			

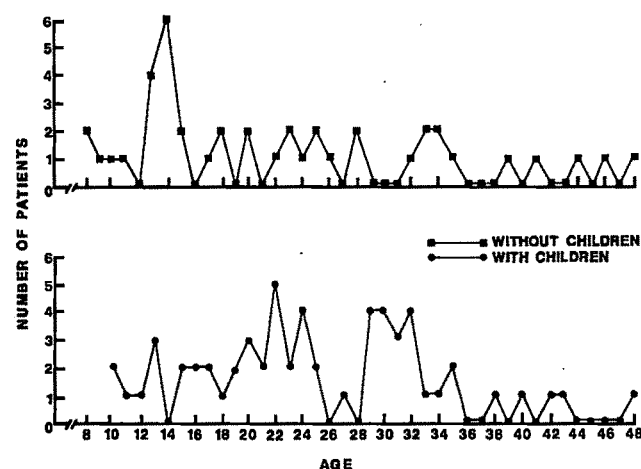
^aNo children from other pregnancies.^bActual age.

None of these studies specifically investigated the onset of obsessive-compulsive disorder during the gestation period. While causality is not implied, on the basis of clinical observation we believe that pregnancy is an important life event that may hasten the onset of obsessive-compulsive disorder. The purpose of this study was to investigate the onset of symptoms during gestation.

METHOD

The participants in this study were 106 female patients who had been diagnosed as having obsessive-compulsive disorder according to *DSM-III-R*. Each patient was first diagnosed by a psychiatrist or licensed psychologist during an initial consultation visit. Later an independent diagnosis was made by the patient's assigned therapist, who was a psychiatrist, psychologist, or assistant psychologist. Finally, the case was presented at an interdisciplinary conference. All patients were seen over 4 years at a private research and treatment center that serves people from all social strata. The facility specializes in the treatment of obsessive-compulsive disorder and served more than 500 female patients between 1979 and 1990. Of the 106 female patients, 42 did not have any children and 59 had at least one child each. In addition, four other childless patients had had abortions and one had had a miscarriage; all of these events occurred during the first trimester. The age characteristics of the patients are given in table 1.

To examine the relationship between obsessive-compulsive disorder and pregnancy, the responses of the 106

FIGURE 1. Age at Onset of Obsessive-Compulsive Disorder for Women With (N=59) and Without (N=42) Children

female patients to a set of questions were recorded on a questionnaire developed for this purpose (available on request). The questionnaire assessed age at onset, marital status, number of children, ages at first, second, third, and other pregnancies, and life events associated with onset of obsessive-compulsive symptoms.

The information obtained from the questionnaire and the patients' verbal reports, psychosocial histories, and progress notes were used as the basis of further inquiries about the onset of obsessive-compulsive disorder symptoms during gestation.

RESULTS

As seen in figure 1, the most common age at onset of obsessive-compulsive disorder for women without children was between 13 and 15 years (mode=14 years). Of the 42 women without children, 28.6% (N=12) experienced onset during this period. On the other hand, there were two peaks for the 59 women with children. Because of the bimodal nature of this distribution, it was important to look at the modal ages rather than the mean ages. The first peak appeared at ages 22–24 years, during which 18.6% (N=11) of the women with children experienced onset, and the second peak was between ages 29 and 32 years, during which 25.4% of the women (N=15) first experienced obsessive-compulsive disorder. The mean, median, and modal ages at onset are shown in table 1.

Of the 59 women who had children, 31 (52.5%) were pregnant for the first time between the ages of 22 and 26; of the 37 who had a second pregnancy, 10 (27.0%) were between 23 and 25 and 10 (27.0%) were between 29 and 30; and of the 15 who had a third pregnancy, eight (53.3%) were between the ages of 30 and 33.

Of the 59 patients who had children, only one (1.7%) indicated a decrease of symptoms during the gestation period, whereas 23 (39.0%) each had an onset of illness during gestation. Of these 23 patients, 12

(52.2%) experienced onset with the first child, eight (34.8%) with the second child, and three (13.0%) with the third child. In addition, of the five patients who had abortions or a miscarriage, three experienced the onset of obsessive-compulsive disorder during the time they were pregnant and one had an exacerbation of symptoms. As soon as the pregnancy was aborted, the symptoms disappeared. If the three patients in this group are added to the other women who experienced symptom onset during pregnancy, the percentage of women with onset during this time would rise from 39.0% to 40.6%.

As shown in table 2, 44 patients could not recall any life event that was associated with the onset of obsessive-compulsive symptoms. For many it was a sudden, unexpected occurrence. However, of the life events that were perceived as being important, pregnancy more than any other life event was associated with the onset of obsessive-compulsive disorder. Physical illness was reported to be an important life event during this period by 8.5% of the women without children, and previous panic disorder was reported by 8.5% of the women with children. Other life events that were associated with the onset of obsessive-compulsive disorder by women without children were the death of a loved one, moving, and marital/family stress (4.3% in each case). Three women who did not have children but had had abortions noted that the onset of their obsessive-compulsive symptoms occurred while they were pregnant. After the abortion, which took place in the first trimester, the symptoms disappeared, and years later obsessive-compulsive symptoms appeared again without an associated life event.

DISCUSSION

Certain life events, such as pregnancy, seem to precipitate psychiatric disorders (9). The results of this study indicate that a large percentage (39.0%) of the women with obsessive-compulsive disorder who had children developed the disorder during pregnancy.

Other life events that appeared to be important were previous panic attacks and previous physical illness. The frequency of women who did not associate a particular life event with the onset of their obsessive-compulsive disorder was higher among the women who were childless (55.3%) than among the women who had children (30.5%). This may be partially explained by the fact that many women with children attributed their symptoms to pregnancy, whereas the women without children in general developed obsessive-compulsive disorder at an earlier age and therefore may have been unable to recall any associated major life event.

It is possible that the patients with children and those without children had different developmental histories of obsessive-compulsive disorder. According to figure 1, the patients without children appeared to have a peak onset during puberty and those with children had

TABLE 2. Life Events Associated With Onset of Obsessive-Compulsive Symptoms for 106 Women With and Without Children

Life Event Associated With Onset	With Children (N=59)		Without Children (N=47) ^a	
	N	%	N	%
Pregnancy	23	39.0	0	0.0
Abortion	0	0.0	3	6.4
Miscarriage	0	0.0	0	0.0
Death of a loved one	1	1.7	2	4.3
Panic attacks	5	8.5	2	4.3
Eating disorder	1	1.7	1	2.1
Contact with feces	2	3.4	0	0.0
Operation	0	0.0	1	2.1
Career stress	1	1.7	0	0.0
Sexual abuse	1	1.7	1	2.1
Move	2	3.4	2	4.3
Stopped taking a prescribed pill	1	1.7	0	0.0
Took diet pills	0	0.0	1	2.1
Physical illness	0	0.0	4	8.5
Marital problems	1	1.7	2	4.3
Menstruation	0	0.0	0	0.0
Marriage	1	1.7	0	0.0
Financial stress	2	3.3	0	0.0
None	18	30.5	26	55.3

^aIncludes the five women who had had abortions or a miscarriage.

peaks around the times of their pregnancies, ages 22–24 and 29–32 years. Perhaps the early development of obsessive-compulsive disorder influenced the group without children to remain childless. Many patients commented that they could not entertain the possibility of raising children while being chronically ill.

Childbirth and pregnancy can be stressful. After our study 10 women with children and 10 without were asked about the reasons they chose or did not choose to have children, their levels of stress before, during, and after pregnancy, and their stress levels at pregnancy in comparison with those at other stressful times in their lives. It appears that the women who chose to have children did not view pregnancy as one of the more stressful times in their lives. In fact, they reported being happy during pregnancy. The only stress appeared to be the presence of symptoms of obsessive-compulsive disorder. Those who were childless indicated they did not want children because of the chronicity of their illness and their perceived inability to raise a child and cope with their obsessive-compulsive symptoms at the same time. Of course, the information on stress was all collected retrospectively and the validity of the responses of these women may be questioned.

These initial data suggest that pregnancy may be an important precipitating factor in the onset of obsessive-compulsive disorder. Further research needs to be conducted on risk factors, biological vulnerability, and, if possible, preventive measures that can be taken during early pregnancy.

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New Policy Regarding Letters to the Editor

Effective immediately, Letters to the Editor critical of an article published in the *Journal* must be received within 6 weeks of the article's publication; Letters from outside the United States must be received within 12 weeks. Letters received after the deadline will not be considered and will be returned unreviewed.

Psychiatry and the Homeless Mentally Ill: A Reply to Dr. Lamb

Douglas Mossman, M.D., and Michael L. Perlin, J.D.

Homeless mentally ill persons are highly visible subjects of ongoing public discussion and potent symbols of a host of contemporary social problems. They present psychiatry with a scientific challenge that calls for further elucidation of the sources of their mental illness and for fashioning possible solutions to their problems. They also present a moral challenge that requires psychiatrists to acknowledge the cultural, political, legal, and economic context of the mental problems of the homeless in the course of deciding what should be done to help them. H. Richard Lamb has proposed a program of aggressive outreach and psychiatric hospitalization for the homeless mentally ill. The authors believe that his proposal misconstrues the problems and needs of homeless mentally ill individuals; it would also needlessly infringe upon their freedom, further stigmatize them, and probably not help them. The authors offer an alternative understanding of the plight of the homeless mentally ill which places their problems within a larger context of social trends and domestic issues that society has been reluctant to confront. Psychiatrists can help the homeless mentally ill by championing their liberty rights and by focusing public discourse on the broad national need for improved access to medical and psychiatric care.

(Am J Psychiatry 1992; 149:951-957)

Although mentally ill persons constitute only a minority of the total homeless population (1), they are highly visible subjects of ongoing public discussion and potent symbols of a host of contemporary social problems (2, sections 7.23-7.25). To many observers, the homeless mentally ill are vivid testimony to governmental indifference to the plight of poor citizens; they represent our nation's failure to respond compassionately to its people's needs for shelter, sustenance, and effective medical care. To others, the homeless are a loathsome, monolithic population of crimi-

nals and mentally ill souls negligently released from jails and hospitals, unable to care for themselves, and potentially dangerous to the community (3, 4); they are seen as evidence of public-sector psychiatry's misguided policies and of irresponsible legal advocacy on behalf of hospitalized patients. Former New York City mayor Ed Koch has characterized the last three decades' effort toward deinstitutionalization as one of the "lunacies of government" and regards libertarian attorneys who advocate for patients' rights as "crazies" (5, 6). More sober analyses recognize that deinstitutionalization has not caused homelessness and that the inadequacies of deinstitutionalization stem not so much from the idea itself as from its misexecution over the past two decades, from lack of public consensus about policies for dealing with former hospital patients, and from public mental health systems' failure to offer comprehensive outpatient treatment that could help indigent persons with severe mental illnesses to live in the community (7-9).

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The homeless mentally ill present psychiatry with a twofold challenge. One challenge is scientific, calling on psychiatrists to elucidate the sources of mental illness among the homeless and to describe potential solutions to their emotional problems; this challenge asks psychiatrists what *can* be done to help homeless individuals who are mentally ill. The other challenge is moral, requiring psychiatrists to acknowledge the cultural, economic, legal, and political context of homelessness as it affects judgments about medical issues; this challenge asks psychiatrists to choose, from among many possible courses of action, what they *should* do to help the homeless mentally ill.

In a Commentary published in the *Journal* (10), H. Richard Lamb, M.D., exhorted psychiatrists to "save the homeless mentally ill" through treatment programs combining aggressive community outreach, civil commitment, and involuntary pharmacotherapy. Dr. Lamb was coauthor of the APA task force's recommendations concerning the homeless mentally ill (7). His proposals thus constitute an important conceptualization of this population's problems and of public psychiatry's optimal response. From both a scientific and a moral standpoint, however, we find this conceptualization unsatisfactory. In this Reply, we offer a contrasting conceptualization of the problems of the homeless mentally ill and suggest to psychiatrists what we believe is a more defensible, if more modest, response to these problems.

THE HOMELESS MENTALLY ILL IN SOCIAL CONTEXT

The homeless mentally ill have many problems, two of which are homelessness and mental illness. Although these are problems that are endured by and interact within individuals, the current state of homeless persons who suffer psychiatric symptoms reflects a confluence of social developments and attitudes about the poor and the mentally ill.

Although homelessness is by no means a new phenomenon, contemporary homelessness follows a decade in which all but the wealthiest Americans have experienced, in constant dollars, net decreases in annual income (11). As one of us has discussed in more detail elsewhere (2, 12), four other social developments have contributed particularly to homelessness.

First, the average age of homeless individuals has declined in the last quarter-century. "Baby boomers" have contributed substantial numbers to our cities' homeless populations, as well as special demographic features: they are more likely to use "recreational" drugs, and they also include Vietnam veterans, who themselves comprise a substantial fraction of the homeless (13).

Second, the last two decades have witnessed substantial losses of low-income housing, reflecting the effects of tax abatement programs that encourage urban "gentrification" (1, 14), limited federal funding for subsidized housing (15), and growth-restricting local housing ordinances (16). This has decreased the potential

availability of housing for the poor in general and of specialized housing for the chronically disabled.

Third, the discontinuation of Supplemental Security Income (SSI) benefits that was initiated by the Reagan administration has had a disproportionate impact on persons with mental disabilities (17). Only a fraction of all homeless persons receive government assistance, and their inflation-adjusted median income has declined by two-thirds over the last three decades (18). Although Congressional and Supreme Court actions have caused a partial reversal of this trend (19, 20), the SSI disability system remains a "flawed" and "incoherent" one (21, pp. 915, 964), and the earlier reduction of benefits remains a significant factor in the increased number of homeless individuals (22-25).

Finally, many of the nondisabled homeless had limited work skills and were chronically unemployed before they became homeless (26). As our changing economy provides fewer well-paying industrial-sector jobs for unskilled or semiskilled workers, ethnic minorities are making up an increasing portion of the homeless population (1).

Recent findings consistently deemphasize the significance of deinstitutionalization as a source of homelessness (27). Although a substantial minority of homeless persons might benefit from some form of psychiatric treatment, only a small minority of the homeless need psychiatric hospitalization (28). Those among the homeless who have histories of psychiatric treatment have social backgrounds and characteristics (such as poverty, poor work skills, and lack of housing and social support) that are similar to those of homeless persons without psychiatric histories. It thus seems clear that mental illness is not the primary cause of the plight of the homeless mentally ill (29-31).

The fact that many homeless persons suffer from untreated psychiatric symptoms must be considered in a larger context which recognizes the vulnerability of millions of Americans who have no medical insurance coverage at all, as well as the various forms of discrimination against psychiatric patients that are characteristic of the American health care system. Lack of private health insurance coverage is associated with poor physical health (32) and with elevated prevalences of major mental illnesses (33). Homelessness is, if nothing else, a condition of poverty (34-36), and poor individuals in general are at increased risk for episodes of psychiatric illness (37).

CRITIQUE OF DR. LAMB'S VIEW

Although Dr. Lamb has elsewhere recognized that "homelessness among the chronically and severely mentally ill is symptomatic of the grave problems facing them generally in this country" (38, p. 498), the demographic factors, economic trends, government policies, and social attitudes that contribute to homelessness among the mentally ill received scant attention in his Commentary (10). Dr. Lamb instead offered an indi-

vidually and biologically focused view of their situation and conceptualized their problems in a manner that seems, to use George Engel's terminology (39), strikingly "biomedical."

"A large proportion of the homeless mentally ill," Dr. Lamb wrote, "tend to be resistant to taking psychotropic medications, to treatment generally, and to accepting any living situation." They often lack living situations because they are "too paranoid" or have "disabling functional deficits . . . [that] include disorganized thinking and actions, poor problem-solving skills, and an inability to mobilize themselves due to depression" (10, p. 650). Thus "the great majority" of homeless mentally ill persons need "structure in terms of a controlled living situation" where their taking psychotropic medications can be assured and where "they are given as much freedom as they can handle but not more. For many, this will mean a locked setting" (10, p. 651).

Although he has elsewhere criticized recommendations for massive rehospitalization (40), Dr. Lamb asserted that "outreach teams including psychiatrists should bring all" incompetent homeless persons "to hospitals, involuntarily if need be" (10, p. 650). If the funds necessary for providing high-quality hospital care "are not available, it is more humane to place these patients in [substandard] hospitals . . . than to leave these neglected human beings on the streets" (10, p. 651).

While the efficacy of medication in preventing symptom relapse and rehospitalization of many mentally ill individuals is quite familiar to physicians, so are the limitations of pharmacotherapy, particularly for schizophrenia. A substantial fraction of patients respond poorly to psychotropic medication or relapse while taking maintenance medication (41, 42). Moreover, the long-term outcome for most patients with chronic thought disorders is often characterized by lifelong disability (43, 44). Dr. Lamb's hope that more involuntary pharmacotherapy will substantially alter the lives of the homeless mentally ill ignored these well-established findings.

Dr. Lamb also ignored the attitudes of former public hospital patients toward their involuntary treatment. Although he cited reports suggesting that patients often view their commitment positively, other reports present a contrasting view: refusal of treatment also may reflect a person's knowledge of, or legitimate fears about, the quality of treatment rendered in state hospitals (45-47). A subgroup of the homeless mentally ill shun the public mental health system; they prefer living on the streets to living in institutions and prefer to live with symptoms of mental illness rather than suffer the side effects of medication in state hospital settings (48-50). Some psychiatrists may regard such judgments as evidence of mental illness, but the documented record of abysmal conditions in many state hospitals (17, 51) suggests that some of the homeless mentally ill may be making reasonable choices. Many homeless mentally ill persons *will* accept medication in alternative social settings, such as community shelters (52), and *will* seek medical care in general hospitals (53).

We are puzzled that Dr. Lamb thinks the homeless mentally ill would be helped by aggressive efforts toward involuntary hospitalization. He believes that after "brief hospitalization . . . mentally ill individuals can be placed voluntarily in a suitable living situation" and that a well-staffed and "well-functioning system of case management" might enable chronically ill patients to live in the community and receive needed services and treatment "on a voluntary basis" (10, p. 650). However, he does not "think there's any real evidence that the public is willing to pay for it and that it really could be done in the larger cities where the largest numbers of chronically mentally ill are" (28, p. 7). Elsewhere, one of us has questioned the willingness and competence of our public institutions to respond to the problems of the homeless mentally ill (12). Dr. Lamb seems to agree: "Not only are there insufficient funds to do this but the bureaucracies are too ponderous and inefficient . . . to set up a comprehensive and competent case management system" (10, p. 650). Recent empirical reviews and critical analyses suggest that broadening civil commitment standards results in institutional overcrowding and lessened opportunities for treatment of voluntary patients (45, 46). Also, while there is now federal legislation providing funds to selected programs to aid homeless individuals—the McKinney Homeless Act (54)—it is clear that this act will not be a panacea for any substantial number of the nation's homeless (55).

Dr. Lamb has described the widespread suspicion of and intolerance toward persons with serious mental illness (38), which constitutes another obstacle to their integration into the community after hospitalization. Lack of appropriate disposition is the "single most critical factor which prevents effective service coordination and implementation of rational discharge planning" (16, p. 113). Discriminatory zoning litigation (2, section 7.22; 3), the public's opposition to the insanity defense following John Hinckley's trial (56), and persistent media-reinforced misassociations between violence and mental illness (57) provide just a few of many possible examples of society's "limited tolerance of mentally disordered behavior" (38, p. 499). This kind of stigmatization appears especially pernicious in the face of evidence that patients receiving nonhospital treatment consistently do better than those who are institutionalized (58). There are numerous reports of successful, noninstitutional approaches to the treatment of the chronically mentally disabled in which programs and services providing a sufficient level of social support have enabled such individuals to rejoin the community (12, note 186; 59-62).

WHAT SHOULD PSYCHIATRISTS DO?

Our discussion has emphasized that the problems of the homeless mentally ill result from an interaction of their biological and psychological pathology with social conditions about which psychiatrists should be concerned, but which are not amenable to medical in-

interventions alone (63, 64). The Robert Wood Johnson Foundation Program on Chronic Mental Illness is based on the premise that coordination and improved availability of a full range of community services (including social and vocational rehabilitation as well as outpatient psychiatric treatment) are needed if persons with severe psychiatric disorders are to succeed outside of hospitals (65). A key feature of the program is "the expansion of housing options for people with chronic mental illness" (66). Indeed, Goldman et al. believe that "the Department of Housing and Urban Development's contribution of Section 8 housing certificates" was "the single most powerful motivator for cities to participate" in the program (67, p. 1229).

Goldman et al. also noted that "the need for comprehensive services exceeds the resource capacity of most, if not all, of the sites" participating in the Robert Wood Johnson Foundation program (67, p. 1229). We suspect that this holds true for service systems across the nation. We share Dr. Lamb's skepticism about the likelihood that local, state, or federal governments will soon embrace and provide financial support for the comprehensive systems of social support needed to help poor mentally ill patients succeed in the community. However, we reject Dr. Lamb's suggestion that psychiatrists "work within the limits of what society is willing to pay" (10, p. 650) and encourage the involuntary hospitalization of incompetent homeless individuals.

If society is willing to provide funds only for often-abysmal state hospitals that discharge patients right back to the conditions and situations which led to their need for hospitalization, how would more involuntary hospitalization substantially change matters? (45, 46). Dr. Lamb might argue that under such circumstances, psychiatrists still should do something: administer medication plus "structure" (i.e., involuntary hospitalization and other confinements) to ensure that symptoms resulting from "noncompliance" are minimized. Yet the dictum *primum non nocere* requires physicians to ask themselves how a policy of involuntary hospitalization and an endorsement of stigmatizing (and—if Dr. Lamb is right about society's lack of generosity—probably futile) incarcerations would affect both the homeless mentally ill and the homeless in general. We are concerned that Dr. Lamb's recommendations would reinforce common misperceptions that deinstitutionalization has caused homelessness, that all of the homeless are disturbed and incompetent, and that the public mental health system is to blame for, and therefore can "solve," the problem of homelessness—all the while abetting, justifying, and reinforcing society's reluctance to examine the fundamental economic and social questions underlying homelessness.

Appelbaum sagely noted that courts and legislatures have often evinced "the universal human desire for someone else to make the hard decisions" (68, p. 762) in their willingness to let psychiatrists resolve difficult legal issues. Local, state, and federal governments also may be tempted to let psychiatrists provide solutions (e.g., institutionalization) to the complex and embar-

assing problems of the homeless. Society may approve of psychiatric outreach teams' removing the homeless mentally ill to hospitals, but this practice could obscure physicians' traditional allegiance to individual, consenting patients who seek their services. Providing a "clinical" solution—involuntary hospitalization—to the problems of the homeless mentally ill reinforces psychiatrists' role in performing an already onerous "duty": the authorization of preventive detention (69). As Aviram cautioned, "We must be aware of the potential collusion between the state bureaucracy and psychiatry that may be at the expense of the recipients An unbalanced need for treatment-medical model of mental commitment may lead psychiatry into . . . a role of social control agents" (70, p. 175).

Rather than offering simplistic, medical "solutions" for individuals already cursed by especial social prejudice, psychiatrists should redirect public attention toward the manifold social problems that are the important causes of homelessness in general. They can point out that many homeless persons are interested in receiving psychiatric treatment, but they understandably put a higher priority on meeting their basic material needs (71). Psychiatrists can emphasize the APA task force's view that addressing "the problems of the homeless mentally ill must begin with provisions for meeting their basic needs: food, shelter, and clothing" (7, p. 5) and can remind the public that "providing psychiatric services to a mentally ill homeless person leaves the person still homeless, just as providing food to a hungry homeless person leaves the person still homeless" (72, p. 213).

If they are interested in having society view the mentally disabled with respect and if they want their patients and their specialty to be free of the stigma associated with psychiatric practice, psychiatrists should champion a view of mentally ill persons that emphasizes the same liberty rights for them as are assumed for persons with other medical disorders. Adults generally are under no obligation to attend to their medical problems; they can smoke, overeat, fail to exercise, and otherwise neglect their health because they have a fundamental right to be left alone (73, 74). What ethicists have termed an "implicit contract" forms the basis of the doctor-patient relationship; a person's voluntary decision to seek medical help ordinarily permits creation of the treatment relationship (75). It is sad and frustrating when any individual pointlessly suffers significant symptoms that might respond to medical treatment, yet we must accept this as the consequence of conforming medical practice to general social norms concerning the protection of individual freedom and dignity.

Throughout his discussion, Dr. Lamb referred to homeless mentally ill persons who are "resistant" to accepting treatment as "patients." To emphasize the benefits and efficacy of treatment, psychiatrists might better refer to obviously troubled and untreated street people as "nonpatients." This designation indicates that such individuals are not receiving care that could alleviate symptoms but acknowledges their presumed

right to make their own decisions, even if those decisions are not the ones that doctors would recommend.

Increasingly, it is suggested that reinstitutionalization would help solve the problem of the homeless. In responding to this assertion, psychiatrists should keep in mind that "homelessness has become a public policy battleground" (72, p. 212). Although mental health systems and civil libertarians are convenient targets for those who wish to make accusations or assign blame, homelessness is a complex problem for which all citizens ultimately share responsibility. Psychiatrists surely share responsibility for some aspects of the problem of homelessness, and they can demonstrate a constructive public response by acknowledging their profession's failings without being unduly defensive. Psychiatrists can also demonstrate their maturity by resisting the temptation to counterblame attorneys or courts that have affirmed psychiatric patients' rights and by resisting the temptation to provide the whole solution to a problem for which they bear only a small portion of the responsibility.

Psychiatrists also could respond by reminding the public that only a minority of the homeless have severe psychiatric disorders, that only a small fraction of the homeless are incompetent to make decisions about their need for hospitalization, that incompetence is a legal status which judges, not psychiatrists, determine (51, 76), and that, ultimately, homelessness is a problem of poverty and resource distribution. Incompetence and mental illness are, of course, not identical. Psychiatrists should underscore their expertise in the latter and reinforce the role of courts in adjudicating the former. They should emphasize that the nature and duration of the confinement of noncriminals, and the method for determining who among the mentally ill should be deprived of liberty, remain legal issues (77, 78). Doing so would also emphasize psychiatrists' presumption of respect for individuals' decision-making power and their endorsement of the same contractual model of treatment that is presumed for nonpsychiatric conditions.

Finally, psychiatrists can join Peele (79) in championing private office practice as the preferred locus of psychiatric care, including care of individuals whose treatment traditionally is relegated to the public sector. The availability of psychiatric outpatient treatment on a par with other office treatment is conducive to the spending of health care dollars on treatment itself (as opposed to institutional custody) and can assure patients' access to the pharmacologic and psychotherapeutic advances that psychiatry has witnessed over the last two decades (79). Psychiatrists in private practice could offer to provide services to homeless persons by setting aside a portion of their time to see persons at shelters or other facilities that serve the homeless. In doing this, careful thought should be devoted to establishing treatment "parameters" so that patients would not be (or feel) coerced into seeing psychiatrists, and psychiatrists would not feel pressured to coerce patients into accepting unwanted forms of treatment. All persons with psychiatric disturbances (including the homeless mentally ill)

should be granted the autonomy typically accorded to persons who seek medical treatment in general, including a contractual relationship with a physician of one's choosing and the rights, privacy, and dignity characteristic of office practice.

CONCLUSIONS

Maimonides offered guidance for those perplexed by the plight of the homeless mentally ill:

Anticipate charity by preventing poverty; assist the reduced fellowman, either by a considerable gift, or a sum of money, or by teaching him a trade, or by putting him in the way of business, so that he may earn an honest livelihood, and not be forced to the dreadful alternative of holding out his hand for charity. This is the highest step and the summit of charity's golden ladder. (*Charity's Eight Degrees*, quoted in 80, p. 74)

Psychiatry's understanding of the central role of self-esteem in emotional life (81) need not be abandoned when we contemplate homelessness and mental illness. In both their care of individuals and their contribution to public discourse, psychiatrists can best serve the liberty rights and the emotional needs of the homeless mentally ill through a *prima facie* affirmation of the legitimacy of their wishes and by helping the general public gain insight into the underlying social problems of which homeless mentally ill persons are vivid and unfortunate victims.

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Regulation of Appetite and Cholecystokinin Secretion in Anorexia Nervosa

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Six patients with anorexia nervosa, the same patients after weight normalization, and six healthy control subjects had similar fasting and postprandial plasma cholecystokinin concentrations. These data do not support the hypothesis that low levels of hunger and food intake in anorexic patients reflect hypersecretion of this endogenous hormone, which is thought to inhibit hunger, promote satiety, and reduce feeding.

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Studies in experimental animals (1,2) show that cholecystokinin in both the CNS and periphery promotes satiety during feeding. Studies in human volunteers (3,4) also support a satiety-inducing role for peripherally secreted cholecystokinin. In this regard, we have shown (3) that the secretion of cholecystokinin into plasma during a meal strongly correlates with satiety in healthy volunteers. We also observed (3) abnormally low endogenous cholecystokinin release after eating in bulimic women, and the magnitude of this impairment correlated significantly with impaired postprandial satiety. We postulated that this impairment in meal-related plasma cholecystokinin might reflect an intrinsic defect that predisposed patients with bulimia nervosa to pathological eating behavior or that it might be a consequence of abnormal eating behavior which was perpetuating the illness.

In the present study we sought to determine whether patients with anorexia nervosa have abnormally high plasma cholecystokinin concentrations, which might be contributing to their pathologically restricted eating.

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We restudied each anorexic patient after correction of her weight loss to explore whether the cholecystokinin response to feeding was related to body weight in our cohort.

METHOD

Subjects

Six female patients with anorexia nervosa were studied, and all six were again studied several months later, 3-4 weeks after restoration of their ideal weights (3). Three of these patients had histories of sporadic binge eating. The control subjects were six age- and sex-matched volunteers in good health and without personal or family histories of eating disorder, affective disorder, alcoholism, or schizophrenia. All normal subjects were within 10% of their ideal body weights (3). All patients and control subjects were medication free and did not smoke. The mean age of both the patients and control subjects was 24 years (SD=5 and SD=4, respectively). The mean duration of anorexia in our patients was 6 years (SD=5). Mean body weight was 37.3 kg (SD=3.5) in the anorexic patients and 56.0 kg (SD=6.2) in the normal subjects. After refeeding, the patients' mean weight increased to 52.6 kg (SD=3). All subjects gave informed, written consent before participating in the study, which was approved by the National Institute of Mental Health Committee on Human Subjects.

Procedure

The subjects adhered to a controlled low-monoamine diet. Each subject was studied in the morning after an overnight fast. Blood samples were drawn through an indwelling 21-gauge intravenous catheter in the antecubital fossa and collected into iced heparinized tubes at various times before and after consumption of the test meal, and they were immediately centrifuged at 4 °C to obtain plasma for cholecystokinin determination.

After the postfast samples were obtained, the subjects were each fed 7 ml/kg of a vanilla-flavored mixed liquid meal. The meal consisted of one egg, half-and-half (milk and cream), and a commercial powdered instant breakfast supplement. The meal contained 1.6 calories/ml and had a macronutrient composition of 40% fat, 20% protein, and 40% carbohydrate. Each subject consumed the entire meal within 2 minutes, except patient 5 during the low-weight phase. This subject consumed only 2 ml/kg of the test meal and adamantly refused more, tearfully complaining of nausea. This patient was thus again given only 2 ml/kg of the test meal during her weight-recovered study. She had no difficulty in consuming this second meal. One matched control subject was also fed 2 ml/kg of the test meal.

Hunger and satiety were assessed with 100-mm visual analogue scales, which included distractors (3).

Cholecystokinin concentrations in plasma were measured by a specific and sensitive bioassay, which has been extensively validated (5). Briefly, cholecystokinin was absorbed onto Sep-Pak cartridges and dried under nitrogen, and cholecystokinin bioactivity was measured with isolated rat pancreatic acini. The minimal detection limit was 0.2 pmol/liter. The recoveries of cholecystokinin-8 and cholecystokinin-33 added to charcoal-stripped plasma were 92% (SD=6%) and 85% (SD=10%), respectively. The intra- and interassay coefficients of variations were 8.6% and 12.7%, respectively.

Statistical Analysis

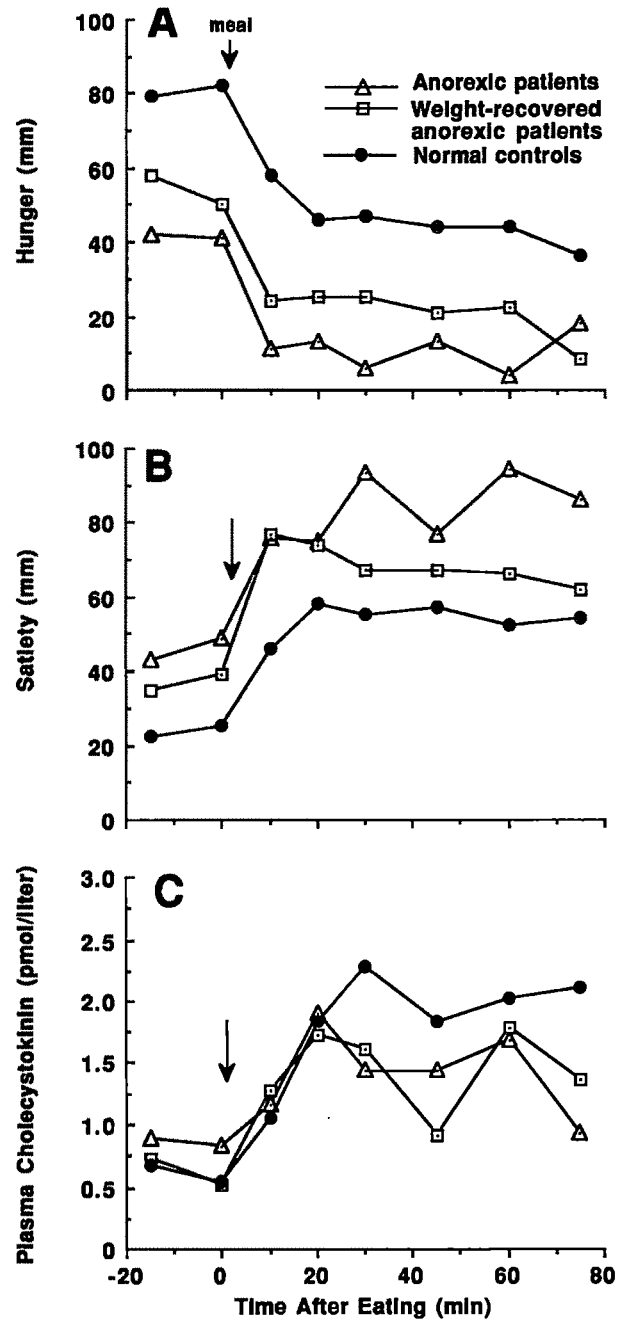
Net cholecystokinin response was calculated as total area under the concentration-time curve, minus the mean basal value multiplied by 75 minutes. Group comparisons were analyzed with the Student's two-tailed *t* test. For longitudinal comparisons of the same patients the two-tailed paired *t* test was used. All values are expressed as the mean and standard deviation of the mean.

RESULTS

Hunger and Satiety Ratings

Ratings of hunger and satiety before and after the test meal are shown in figure 1. We calculated a mean basal rating for each group on the basis of the values at -15 and 0 minutes, and mean postprandial ratings were

FIGURE 1. Fasting and Postprandial Levels of Hunger, Satiety, and Plasma Cholecystokinin in Patients With Anorexia Nervosa Before and After Weight Recovery and in Normal Control Subjects^a



^aThe arrow indicates the beginning of the meal. Hunger and satiety were rated on 100-mm visual analogue scales; cholecystokinin is expressed as cholecystokinin-8 equivalents.

based on all of the values after the beginning of the meal. The mean basal (fasting) hunger sensation, as rated on the 100-mm visual analogue scale, was 43 mm (SD=37) for the underweight patients with anorexia nervosa and 82 mm (SD=13) for the normal control subjects ($t=2.36$, $df=10$, $p<0.05$) (figure 1, part A). After the correction of their weight loss, the mean basal

hunger rating of the anorexic subjects was still somewhat lower than the control value: 49 mm (SD=38) versus 82 mm (SD=13) ($t=1.91$, $df=10$, $p<0.10$). After consumption of the test meal, the mean hunger rating was much lower for the underweight anorexic subjects than for the control subjects—10 mm (SD=16) versus 46 mm (SD=13) ($t=4.2$, $df=10$, $p<0.05$)—but after weight correction the patients' rating of postprandial hunger rose to 23 mm (SD=32), which was not significantly different from control values ($t=1.99$, $df=5$, $p=0.10$) (figure 1, part A). However, the normal subjects, the anorexic patients, and the weight-corrected patients showed similar mean reductions in hunger ratings after the consumption of the test meal: 35 (SD=19), 31 (SD=38), and 26 (SD=38) mm, respectively.

The mean basal satiety ratings were 26 mm (SD=17) for the control subjects, 48 mm (SD=34) for the underweight anorexic patients ($t=1.40$, $df=10$, n.s.), and 39 mm (SD=25) for the anorexic patients after short-term weight normalization ($t=1.02$, $df=10$, n.s.) (figure 1, part B). The mean postprandial satiety ratings were 53 mm (SD=13) for the healthy subjects and 78 mm (SD=35) for the underweight anorexic patients ($t=1.65$, $df=10$, $p=0.13$). After correction of their weight loss, the anorexic patients had a mean postprandial satiety rating of 68 mm (SD=26); the difference from the rating when they were underweight was nearly significant ($t=2.17$, $df=5$, $p=0.08$). The mean postprandial changes in satiety were similar in all subject groups, averaging 27 (SD=23), 31 (SD=44), and 30 (SD=28) in the healthy subjects, underweight anorexic patients, and patients after weight restoration, respectively (figure 1, part B).

Plasma Cholecystokinin

The basal fasting plasma cholecystokinin concentrations were similar in all groups, averaging 0.6 pmol/liter (SD=0.2) in the control subjects, 0.9 pmol/liter (SD=0.8) in the underweight anorexic patients ($t=0.83$, $df=10$, n.s.), and 0.6 pmol/liter (SD=0.3) in the anorexic patients after weight recovery ($t=0.27$, $df=10$, n.s.) (figure 1, part C). Similarly, no significant differences between subject groups in peak postprandial plasma cholecystokinin concentrations were observed. The mean peak levels were 2.9 pmol/liter (SD=1.1) in the healthy subjects, 2.2 pmol/liter (SD=1.4) in the anorexic patients, and 2.3 pmol/liter (SD=1.7) in the anorexic patients after the short-term weight correction (data not shown). Furthermore, the net integrated cholecystokinin responses during test meal administration were similar: 100 pmol/liter-min (SD=52) in the control subjects, 73 pmol/liter-min (SD=67) in the underweight anorexic patients ($t=0.79$, $df=10$, n.s.), and 73 pmol/liter-min (SD=59) in the anorexic patients after weight correction. However, the anorexic group experienced great intraindividual changes in cholecystokinin secretion between the low-weight and weight-corrected conditions. The two patients with the lowest cholecystokinin responses to feeding while at low weight, both of whom had histories of sporadic binge eating, had the highest

responses after weight normalization, and the two patients with the most robust cholecystokinin responses while at low weight, both of whom had pure restricting-type anorexia, had blunted responses after refeeding. One anorexic subject (patient 5) had high fasting plasma cholecystokinin concentrations (averaging 2.5 pmol/liter) while underweight, which fell to 0.5 pmol/liter while fasting after weight normalization.

Glucose and Urinary Ketones

The fasting glucose levels in all subjects were normal, ranging from 71 to 90 mg/dl. No urinary ketones were detectable in any subject, including the low-weight anorexic patients.

DISCUSSION

Like previous investigators (6, 7), we found that patients with anorexia nervosa experienced more satiety and less hunger while fasting and after eating than did normal subjects. These appetite abnormalities were ameliorated by short-term weight correction. At the same time, there were no differences between anorexic patients, the same patients after weight recovery, and healthy control subjects in the mean postprandial changes in hunger and satiety. This observation is compatible with our finding of similar postprandial cholecystokinin concentrations in all the subject groups. These results are in line with the normal postprandial cholecystokinin-33 concentrations previously reported in eight patients with anorexia nervosa, studied only in the underweight state (8).

Despite their profound weight loss and lack of hunger, the underweight patients with anorexia nervosa had normal basal plasma concentrations of cholecystokinin. This finding, combined with the finding of normal postprandial concentrations of the hormone in anorexia, does not support the hypothesis that low hunger levels in anorexic patients are due to abnormally high cholecystokinin secretion (9). However, our finding of high basal cholecystokinin concentrations, which normalized after weight restoration, in a single patient suggests that lack of appetite while fasting might be associated with inappropriate cholecystokinin secretion in a subgroup of patients. Larger studies will be required to assess this possibility.

We cannot rule out the possibility that greater than normal end organ sensitivity to cholecystokinin is involved in the high satiety ratings and low hunger ratings in anorexic patients. Hypercortisolemia, for example, might sensitize certain end organs to the effects of cholecystokinin (10). Use of specific cholecystokinin receptor antagonists will be required to address this issue. Furthermore, since cholecystokinin release is stimulated by delivery of nutrients into the duodenum, assessment of gastric emptying would be helpful in interpreting meal-stimulated cholecystokinin concentrations in plasma. Thus, if delayed gastric emptying were to be found in

anorexic patients in combination with normal cholecystokinin secretion, then even the normal cholecystokinin concentrations might be considered inappropriately high.

It is interesting that the significant enhancement of hunger and reduction of satiety observed in the anorexic patients after correction of their weight loss was not associated with any group change in cholecystokinin secretion, leaving open the possibility that cholecystokinin secretion in anorexic patients is dissociated from their appetitive sensations. In this regard, large, seemingly unpredictable intraindividual changes in cholecystokinin secretion between the low-weight and weight-corrected conditions were observed in the anorexic patients. The meaning of this variability in cholecystokinin secretion is unclear; however, it may represent an area of physiologic instability in anorexia nervosa, perhaps related to the predisposition of many anorexic patients to alternate between food restriction and binge eating. Detailed, longitudinal studies are needed to assess this possibility.

In summary, these findings indicate that, in contrast to patients with bulimia nervosa, the majority of patients with anorexia nervosa have normal fasting and postprandial plasma cholecystokinin levels. There were no observable relationships between body weight, nutritional status, and meal-provoked cholecystokinin secretion in this study. Accordingly, these data do not support the hypothesis that low hunger levels and high satiety ratings in patients with anorexia nervosa are due to hypersecretion of cholecystokinin into plasma,

although a small subgroup of anorexic patients with inappropriate cholecystokinin secretion may exist.

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Replication of Action of Cholecystokinin Tetrapeptide in Panic Disorder: Clinical and Behavioral Findings

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Eleven patients with panic disorder were challenged with cholecystokinin tetrapeptide (CCK-4) on two occasions. The effects of CCK-4 were consistent except symptom onset was more rapid with the second injection. Demonstrating that the effects of CCK-4 are reproducible in panic patients opens the door for studies of the effects of drug treatment on CCK-4-induced panic.

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Recent studies (1-3) suggest that cholecystokinin tetrapeptide (CCK-4) could provide a pharmacologic model of panic attacks in humans. This is supported by findings that CCK-4 satisfies four criteria for a panicogenic agent: it seems safe for use in humans, it elicits both somatic and affective symptoms of a panic attack, it induces attacks that are similar to patients' usual attacks, and it precipitates panic attacks at a higher frequency in patients than in normal subjects.

To further establish the relevance of CCK-4 as a model anxiety- and panic-inducing agent, it is important to verify whether its effects are consistent and reproducible in multiple administrations. Fulfilling this criterion is essential for eventual studies of the effects of antipanic drugs, such as imipramine and alprazolam, on CCK-4-induced symptoms.

METHOD

Patients with DSM-III-R panic disorder with or without agoraphobia were selected from an anxiety disorders clinic. Other criteria were age between 18 and 65 years, good physical health, and at least two panic attacks per week for 3 weeks before entrance into the study. Low doses of benzodiazepines were permitted

throughout the study provided that the doses were not altered. The patients provided written informed consent for their participation, and the study was approved by appropriate ethical review boards.

The group included four men and seven women (median age=42 years, range=24-61). The median number of panic attacks during the week before the study was 10.0 (range=2-35), and the median duration of illness was 6.0 years (range=2-25). Eight patients were taking benzodiazepines at the time of the study: alprazolam, N=4 (mean dose=0.66 mg/day, SD=0.5); clonazepam, N=2 (mean dose=1.5 mg/day, SD=0.7); lorazepam, N=1 (2 mg/day); clonazepam plus lorazepam, N=1 (1 mg/day and 2 mg/day, respectively). These regimens did not change during the study, and the time of the last dose was kept constant.

We prepared the CCK-4, consisting of an amino acid chain of Trp-Met-Asp-Phe-NH₂, according to procedures published earlier (1). The patients were challenged with 25 µg i.v. of CCK-4 in a bolus push on two occasions, separated by a 2-3-day interval. On each occasion, the patient first received one injection of placebo (2.5 ml of 0.9% NaCl) followed by one injection of CCK-4 (injected in 2.5 ml of 0.9% NaCl). The second injection (CCK-4) was administered after the patient fully recovered from the first injection (placebo). The patients were blind to the order of the injections.

Immediately after each injection the patient was asked to describe the symptoms experienced since the injection. The onset, duration, and description of these symptoms were recorded by one of the investigators. On a scale of 0-4, each patient rated the intensity of the symptoms on a symptom checklist derived from DSM-III-R. Symptoms not appearing on the checklist but spontaneously reported by patients were also rated. The patient was then asked to compare the response to CCK-4 with clinical attacks and to report whether any novel symptoms had occurred with CCK-4. Two vari-

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TABLE 1. Symptoms Induced by Cholecystokinin Tetrapeptide (CCK-4) and Placebo in 11 Patients With Panic Disorder

DSM-III-R Symptom	Intensity of Symptom (range=0-4)								Solution Effect	
	Session 1				Session 2					
	CCK-4		Placebo		CCK-4		Placebo			
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F (df=1, 10)	p
Dyspnea ^a	2.3	1.6	0.9	1.4	2.1	1.8	0.4	1.0	13.38	<0.01
Palpitations/rapid heartbeat	2.0	1.5	0.4	1.0	1.4	1.6	0.6	1.0	14.14	<0.01
Sweating	2.0	1.4	0.5	1.0	2.2	1.5	0.1	0.3	22.04	<0.001
Faintness	1.6	1.8	0.5	1.2	1.7	1.4	0.4	1.2	15.51	<0.01
Unsteadiness	1.9	1.4	0.8	1.6	1.9	1.6	0.4	1.2	15.25	<0.01
Dizziness	1.5	1.5	0.9	1.4	1.4	1.4	0.5	1.2	8.71	<0.05
Shaking/trembling	1.4	1.8	1.0	1.7	1.2	1.7	0.4	1.2	—	n.s.
Nausea	1.4	1.6	0.2	0.6	1.7	1.6	0.2	0.6	10.70	<0.01
Abdominal distress	1.8	1.5	0.0	0.0	1.5	1.7	0.4	0.7	15.00	<0.01
Choking	2.0	1.5	0.4	0.7	1.9	1.6	0.5	1.0	12.69	<0.01
Chest pain/discomfort	1.4	1.4	0.3	0.6	1.6	1.7	0.4	0.9	10.50	<0.01
Paresthesia	1.6	1.6	0.6	1.2	2.1	1.6	0.0	0.0	14.41	<0.01
Hot flushes/chills	2.2	1.3	0.6	1.2	2.2	1.7	0.1	0.3	25.72	<0.001
Unreality/detachment ^a	1.4	1.6	0.9	1.6	1.2	1.7	0.3	0.9	7.57	<0.05
Anxiety/apprehension/fear	2.6	1.0	0.8	1.3	2.5	1.7	0.8	1.3	33.95	<0.001
Fear of dying	0.8	1.5	0.1	0.3	0.9	1.6	0.1	0.3	—	n.s.
Fear of losing control	1.5	1.7	0.5	1.3	1.3	1.7	0.3	0.9	6.29	<0.05
Fear of going crazy	0.9	1.6	0.4	1.2	0.8	1.5	0.3	0.9	—	n.s.

^aSignificant session effect for dyspnea ($F=9.80$, $df=1, 10$, $p<0.05$) and unreality/detachment ($F=5.38$, $df=1, 10$, $p<0.05$) (two-tailed probability).

ables were obtained from the checklist: 1) a score for the total number of symptoms (number of items scored 1 or higher) and 2) a sum intensity score (sum of intensity ratings of symptoms). To be defined as a panic attack, the symptoms had to meet the DSM-III-R criteria, including both somatic and affective symptoms of a panic attack, and had to be reported by the patient as a panic attack.

RESULTS

None of the symptoms induced by CCK-4 was reported as novel by any of the patients. The mean numbers of symptoms for the first and second sessions were, respectively, 11.8 (SD=4.0) and 11.2 (SD=5.2) for CCK-4 and 4.2 (SD=6.2) and 3.3 (SD=4.8) for placebo. The symptom intensity sums were 31.6 (SD=17.6) and 32.0 (SD=21.4) for CCK-4 and 11.2 (SD=17.8) and 6.5 (SD=13.4) for placebo. A Solution by Session analysis of variance with repeated measures revealed no significant difference between the initial and second challenge sessions in the number of symptoms ($F=1.31$, $df=1, 10$, $p<0.28$) or intensity sum ($F=1.21$, $df=1, 10$, $p<0.30$), regardless of solution administered (interactions were nonsignificant). In contrast, the number of reported symptoms ($F=86.10$, $df=1, 10$, $p<0.000$) and the symptom intensity sum ($F=55.46$, $df=1, 10$, $p<0.000$) were significantly higher with CCK-4 than with placebo for both sessions. A breakdown of symptoms induced with CCK-4 and placebo appears in table 1.

Changes in the onset and duration of symptoms were evaluated for CCK-4 only, by means of paired t tests. No significant increases or decreases in the mean duration of symptoms were found between the initial and

second injections: 5.8 (SD=4.8) versus 5.2 (SD=4.8) minutes ($t=1.25$, $df=10$, $p<0.24$), but the time before onset of symptoms was significantly shorter with the second CCK-4 injection: 26.3 (SD=7.2) versus 20.9 (SD=3.8) seconds ($t=2.77$, $df=10$, $p<0.02$).

The prevalences of panic attacks after the first and second CCK-4 injections were similar. The rate of panic was significantly greater with CCK-4 than with placebo for both sessions ($p<0.01$, binomial tests). In the initial challenge session, nine (81.8%) of the 11 patients panicked with CCK-4 and one (9.1%) panicked with placebo. In the second session, eight (72.7%) patients panicked with CCK-4 and one panicked with placebo. Eight patients (72.7%) panicked with both CCK-4 injections, and one panicked with both placebo injections.

DISCUSSION

This study demonstrates that the behavioral effects of CCK-4 are reproducible in patients with panic disorder. The main difference between testing sessions was that the onset of CCK-4-induced symptoms was more abrupt in the second session. This may be explained by a neuronal sensitization induced by CCK-4 or by an earlier recognition by patients of symptoms induced by the second CCK-4 injection. Further studies are needed to clarify this point.

Demonstrating that the effects of CCK-4 are reproducible in panic patients opens the door for studies on the effect of treatment with imipramine, alprazolam, or experimental drugs on CCK-4-induced panic. In animal models (4-8), CCK-4 is anxiogenic, its effects are antagonized by CCK receptor antagonists, and CCK an-

tagonists are anxiolytic. Research using the test-retest design reported here is now needed to evaluate whether CCK receptor antagonists can block the panicogenic effects of CCK-4 in panic disorder patients, and studies are needed to evaluate the therapeutic potential of CCK receptor antagonists.

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Somatic Symptoms After a Natural Disaster: A Prospective Study

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The authors prospectively examined the prevalence of somatization symptoms among community respondents after a natural disaster in Puerto Rico. Exposure to the disaster was related to a higher prevalence of medically unexplained physical symptoms, particularly gastrointestinal ones (abdominal pain, vomiting, nausea, excessive gas) and pseudoneurological ones (amnesia, paralysis, fainting, unusual spells/double vision).

(Am J Psychiatry 1992; 149:965-967)

Although the psychiatric literature consistently points to increased morbidity among persons exposed to disasters, most previous studies have not used structured formats or have been retrospective. In the only previous prospective study (1), the reinterviewing, with a structured interview, of subjects exposed to a series of disasters in St. Louis afforded a longitudinal view of the impact of disasters and revealed that such disasters were unlikely to initiate mental disorders or affect levels of new psychiatric symptoms. In that study, 43% of the subjects exposed to the disasters and 25% of those who were not exposed reported at least one new somatization symptom. Although not statistically significant, this observation was of interest to us, since we had theorized that somatic symptoms may serve as coping mechanisms or reflect enduring traits (2). A natural disaster affecting respondents who had been previously interviewed with a structured interview presented an opportunity to perform a prospective study to test these hypotheses further.

On Oct. 6 and 7, 1985, Puerto Rico was hit by severe flash floods and mudslides. This was one of the worst five such disasters affecting U.S. territories in the last two decades; it left at least 180 persons dead and thousands injured (3). The disaster occurred about a year after interviews had been completed as part of a Puerto Rican epidemiological survey (4).

METHOD

In the Puerto Rican survey, which used methods quite similar to those of studies in the United States, 1,551 adult respondents were interviewed in 1984 with a Spanish version of the Diagnostic Interview Schedule (DIS) (4). In 1987, about 1 year after the disaster, 912 respondents were interviewed with the same research instrument. Of these, 41% (N=375) were part of the original cohort interviewed in 1984. For this article, only data on the 375 respondents who were interviewed both before and after the disaster are included.

Three degrees of exposure (severe, moderate, and minimal) were defined on the basis of self-reports documenting the intensity of direct exposure to the disaster and the occurrence of calamities such as the death of a loved one, serious physical injury, or imminent physical threat to oneself or one's family. Of the 375 respondents interviewed twice with the DIS, 139 were classified as having been exposed to the disaster (they lived in the affected areas, experienced losses, or faced serious risk), and the remaining 236 were classified as unexposed.

In Puerto Rico, an aggregate of 12 somatic symptoms has been empirically derived from the DIS with the use of multivariate analyses (5). These include four pseudoneurological, four cardiorespiratory, and four gastrointestinal symptoms. For the statistical analyses reported in this article, we merged the data on the respondents with severe, moderate, and minimal exposure to the disaster (the exposed group) and contrasted them with the data on the unexposed respondents. We included only data on the 12 somatic symptoms and examined whether these symptoms were new or persistent. A new somatization symptom was defined as a symptom that was reported absent in 1984 but present in 1987; a persistent symptom was defined as one that was reported

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TABLE 1. Respondents Reporting New or Persistent Somatization Symptoms About 1 Year After a Disastrous Storm in Puerto Rico

Type of Symptom	Patients Reporting Symptom				χ^2 (df=1) ^a	p
	Exposed to the Disaster (N=139)		Unexposed to the Disaster (N=236)			
	N	%	N	%		
Gastrointestinal						
New	32	14	23	10	11.28	0.0007
Persistent	11	8	11	5	1.14	0.29
Pseudoneurological						
New	15	11	10	4	5.03	0.02
Persistent	0	0	5	2	—	0.16 ^b
Cardiorespiratory						
New	27	19	39	17	0.33	0.57
Persistent	13	9	13	6	1.45	0.23
Any one symptom						
New	50	36	68	29	1.76	0.18
Persistent	22	16	25	11	1.73	0.19

^aWith Yates' correction.^bFisher's exact test (chi-square may not be applicable because of the low N in each cell).

present in both the 1984 and 1987 interviews. To be scored as present, a symptom had to meet severity criteria and, after probing by the interviewer, be judged unrelated to physical illness, physical injury, or the use of medication, drugs, or alcohol.

In the analyses, numbers of exposed and unexposed subjects reporting at least one new or persistent symptom were compared. Both new and persistent symptoms were broken down into pseudoneurological, cardiorespiratory, and gastrointestinal categories. Significant differences were established with the use of chi-square tests with Yates' correction.

RESULTS

Table 1 shows the number of exposed and unexposed respondents presenting any new or persistent somatization symptom at the time of the second interview. Overall, a higher proportion of exposed than unexposed subjects reported new or persistent symptoms. However, the only statistically significant differences were for new gastrointestinal and pseudoneurological symptoms. Thus, as shown in table 1, both types of new symptoms were more likely to be reported by subjects exposed to the disaster than by unexposed subjects.

DISCUSSION

Studies using the DIS have shown that when the same respondents are interviewed twice, about a year apart, there is a tendency to underreport symptoms in the second interview relative to the first (6). In contrast to such studies, we have demonstrated net increases in somatic and other types of psychiatric symptoms, but only when the second interview follows exposure to a disaster (7).

Our data indicate that somatic symptoms are an important component of the disaster-reactive psychopatho-

logical repertoire and that gastrointestinal and pseudoneurological ones are the most likely to emerge after exposure to a stressor. Gastrointestinal symptoms (abdominal pain, nausea, vomiting, excessive gas) are the somatic symptoms most commonly reported by community populations. Due in part to their high prevalences, these symptoms tend to be rather nonspecific. For example, increases in these symptoms may reflect a variety of psychiatric or physical states, and in the case of natural disasters, it is possible that these symptoms may also result from the unsanitary conditions that often follow such events. Pseudoneurological symptoms (amnesia, paralysis, fainting, and unusual spells/double vision), however, may be more specific indicators of stress responses than other symptoms. For example, these symptoms have low prevalences, have been traditionally linked to psychological distress, and are more commonly related to conversion disorder than to somatization disorder. It is interesting that two of these symptoms, fainting and unusual spells, are common characteristics of *ataque de nervios*, a culture-bound syndrome frequent among Puerto Rican populations and usually related to stressful events.

An advantage of assessing unexplained somatic symptoms as possible indicators of psychopathology among general populations is that they are more objective, easier to elicit, less likely to be subject to misunderstanding, and far less intrusive than questions addressing psychopathology more directly. An obstacle in eliciting these symptoms is their large number (there are 37 in *DSM-III-R*), since they have to be individually scrutinized. Grouping these symptoms on the basis of natural clusters may facilitate this process in the future and allow wider applications of these promising leads to the study of clinical and community populations.

The limitations of the data in this study are those inherent in epidemiological research in psychiatry, such as use of questionnaires administered by lay interviewers and total reliance on respondents' reports. Since Puerto Rico is a relatively small, self-contained area with

a high population density, it is conceivable that almost anyone residing in the island may have been directly or indirectly affected by the disaster. Therefore, differences in symptom presentation between the exposed and unexposed groups may have been attenuated. Also, the sample of exposed subjects was relatively small and the length of time that elapsed between the disaster and the interviews was rather long, so extraneous factors may have influenced the results.

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Book Forum

Nancy C. Andreasen, M.D., Ph.D., Editor

ALCOHOLISM

Understanding and Treating Alcoholism, vol. 1: An Empirically Based Clinician's Handbook for the Treatment of Alcoholism, by Jill Littrell. Hillsdale, N.J., Lawrence Erlbaum Associates, 1991, 408 pp., \$75.00.

Understanding and Treating Alcoholism, vol. 2: Biological, Psychological, and Social Aspects of Alcohol Consumption and Abuse, by Jill Littrell. Hillsdale, N.J., Lawrence Erlbaum Associates, 1991, 311 pp., \$49.95 (\$99.95 for both volumes).

In 1981 Dr. Littrell completed her doctorate in clinical psychology and began working with alcoholics. She heard a great deal of allegedly factual information about alcoholism from both therapists and patients, but, as a scientist, she wondered what was really true. These two volumes are her attempt to give others the empirical findings on alcoholism that she wished were available to her when she began her work with alcoholics more than 10 years ago. She has succeeded admirably. These books are a great addition to the literature on alcoholism and will be an important resource for therapists and researchers alike.

I will mention some of the conclusions from each volume. In volume 1, Dr. Littrell discusses empirical findings relating to Alcoholics Anonymous (AA) as a treatment. Since some see AA as the treatment of choice but others think of it as a substitute illness, it is important to know what the real situation is. Her findings here, like many in the book, show that there are no simple answers, that the results depend on several variables. For example, AA works best, she finds, with alcoholics who are authoritarian, religious, and opposed to controlled drinking. Those who seek out AA tend to be gregarious and to have been better adjusted in childhood than other alcoholics but lacking in social support as adults.

Dr. Littrell notes that there is a high treatment dropout rate among alcoholics. As many as one-third of intake patients fail to return for treatment. Thus, the defensiveness that drug users often display is shown in the failure of alcoholics to engage in treatment, even though they may have gone for an intake interview.

The MMPI is possibly the best personality test in psychology, and the author presents many findings relating to alcoholism and the MMPI. For example, two types of MMPI profiles have been found for wives of alcoholic men. One group seems to be anxious and depressed (elevated profiles on depression, psychasthenia, and hysteria scales), and the other group scores high on the psychopathic deviate scale. In traditional terms, the first group of wives seems to be neurotic and the second group seems to have character disorders. This does not necessarily mean that these women are mentally disordered but, rather, that they show traces of neurotic or psychopathic qualities. Some may be mentally disordered. Also, some may have been this way before they encountered the alcoholic and others may show these patterns in response to living with an alcoholic.

Volume 2 has some important insights that many may not know about. For example, the reader may think that twin studies have either proven the genetic basis of alcoholism or at least can easily do so. However, things are not quite this simple. For one thing, monozygotic twins tend to live in a common residence longer than dizygotic twins, so heredity and environment are confounded. For another, twin studies fail to examine types of alcoholism, such as primary alcoholism, which seems to be independent of additional psychopathology, and secondary alcoholism, which is preceded in time by another primary disorder, such as antisocial personality disorder or depression. Thus, twin studies are not definitive for showing the inheritance of alcoholism, although they tend to support the view that alcoholism is inherited. Even here another caveat is in order: the results for inheritance of alcoholism is clearer in the case of males than it is in the case of females.

Even if alcoholism is an inherited disorder, cognitive and social factors play roles in its development. Dr. Littrell does an excellent job of discussing these variables, which include attitudes and expectancies as well as gender. For example, she reports that the estimated alcoholism rate for males is 10%, compared with 5% for females. Higher rates of alcoholism are found among nonwhites, Protestants, the lower classes, and individuals who are divorced, separated, or single. Thus, it is clear that social factors interact with any inherited tendencies to produce alcoholism.

The findings on alcohol and sexuality are interesting. Both men and women have subjective increases in sexual arousal after drinking alcohol, and this seems due to expectancies as well as to pharmacological effects. Initially, people have greater physical sexual arousal from alcohol, but sexual physiological functioning is reduced with increased dosages. Men drinking an alcohol placebo experience greater penile tumescence, but women do not show greater physical sexual arousal in response to an alcohol placebo. Both men and women show strong subjective reactions to alcohol, indicating the power of expectation. We expect alcohol to make us less inhibited sexually; this is a powerful belief that can serve as a self-fulfilling prophecy.

These two volumes are excellent and will add greatly to the knowledge of anyone concerned with alcohol and alcoholism. The volumes are so good that I recommend them despite their cost.

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CHILDREN AND THE ELDERLY

Disorders of Learning in Childhood, by Archie A. Silver and Rosa A. Hagin. New York, John Wiley & Sons, 1990, 683 pp., \$65.00.

Depending on the definition and the methods used for estimating its prevalence, learning disability is a problem that may

affect between 5% and 30% of schoolchildren. Indeed, at least 5% of all elementary schoolchildren in the United States receive special education services for learning disabilities. This book is about these children as well as others who are academic failures.

In part one, the authors present their argument that the term "learning disorders" rather than "learning disabilities" should be used because it is more descriptive of the population that is the focus of their book. This population includes "all children whose academic achievement is below that expected from their age and intelligence" (p. 25). Thus, the book is very broad in scope and includes children with a number of childhood disorders that typically are not thought to be subsumed under the term "learning disabilities." Further, the authors consider the voluminous data on subtyping of children with learning disabilities and suggest that the unifying concept basic to all subtype differences is the children's difficulties with spatial orientation and/or temporal organization.

In part two, the authors present a rich array of methods, procedures, and protocols based on their years of clinical and research work in the management of children with learning disorders. Included are excellent chapters on educational and psychological assessment and management that present a wealth of information on a wide variety of methods, including a number of new and innovative techniques (e.g., reading recovery). Based on their own experience, the authors recommend a five-step decision-making process to evaluate 1) educational achievement, 2) educational opportunity, 3) sensory acuity, 4) cognitive functioning, and 5) neuropsychiatric functioning. An integration of data from these assessments provides the basis for designing appropriate intervention strategies. There is a chapter on the effects of drugs on learning and memory that includes the traditional medications as well as the nootropics (e.g., piracetam) purported to enhance learning and verbal memory in children with specific learning disability. This is followed by a chapter on psychotherapy that is based mainly on the authors' own casework rather than on the research literature. One suspects that this approach was undertaken because of the dearth of good research on the effects of psychotherapy in this population. Indeed, this points to the need for research in this area. Finally, there is a chapter on prevention of disorders of learning. This is a nice touch because this topic is seldom included in textbooks and, as noted by the authors, prevention has not been an area of much research interest.

Part three deals with clinical patterns in disorders of learning. In six chapters the authors cover the nature, cause, and remediation of such disorders as specific language disability, attention deficit hyperactivity disorder, Gilles de la Tourette's syndrome, and autism. They also include chapters on children who display the effects of poverty, cultural differences, and inappropriate stimulation. Each of the chapters is detailed, draws on knowledge from a number of different disciplines, and provides an integrated framework that will help clinicians to design appropriate treatment protocols. Part four, arguably the best section of the book, presents the authors' vision of future research and services in this field.

This book represents the personal statement of two highly respected clinicians and scholars who have been active in the field of learning disorders for several decades. It is full of descriptions of their own work and that of their colleagues and includes personal communications that date as far back as 1936. It is the sort of book that one would expect from scholars in the twilight of their academic careers—a cross between didactic and academic presentation, with just a hint of dogmatism when it comes to what they consider to be good clinical

practice. It is full of wisdom that comes only from years of clinical experience and dedication to the field.

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Delirium in the Elderly, by James Lindesay, Alastair MacDon-
ald, and Ian Starke. New York, Oxford University Press,
1990, 122 pp., \$45.00.

Psychiatry has been waiting a long time for a book on dementia in the elderly. The result of a collaboration by two psychogeriatricians and a geriatrician (all British), *Delirium in the Elderly* exemplifies the cooperative approach it espouses. A small, readable book of six chapters, it is a pleasing combination of thoroughness and pragmatism, British in its modesty and international in its citations.

Thoroughness is the hallmark of the first chapter, which deals with the concept of delirium. The authors deal here with the issue of definition, which they revisit in the final chapter, which concerns an agenda for research. They point out that we do not yet have an agreed-on definition of delirium and that theoretical difficulties between *DSM-III* and *ICD-10* continue even though they are broadly comparable. These difficulties include the fact that *DSM-III* allows the diagnosis of dementia only when a physical cause can be demonstrated (or, in *DSM-III-R*, presumed) and the fact that *ICD-10* requires that the outcome be known (duration less than 6 months). The authors argue that these difficulties prevent *DSM-III* and *ICD-10* criteria from being used in etiological research. They propose that delirium be strictly regarded as a syndrome and offer their own, less constrained definition.

The second chapter deals with clinical assessment. The advantages of visiting the home are listed, and a schedule for use with informants and a copy of the Mini-Mental State Examination are provided.

The third chapter considers the causes of delirium and is a splendid review of the organic factors. The authors remind us that there is no identifiable organic cause for dementia in a proportion of delirious patients. They observe that psychiatric, psychological, and environmental factors may play a part in delirium and that these may result in physical complications such as dehydration and psychotropic drug use.

The fourth chapter explores the neuronal basis of delirium. It closes with hypotheses regarding hypoactive delirium due to cholinergic dysfunction or due to monoaminergic dysfunction. Hypoactive delirium due to cholinergic dysfunction involves slowing of the EEG, and hypoactive delirium due to monoaminergic dysfunction involves an essentially normal EEG with paroxysmal bursts of fast activity.

The fifth chapter deals with management, including clear and useful diagrams and lists of how to investigate. The section on psychotropic drug treatment is a little too brief, perhaps in an effort to play down the importance of psychotropic medication in dementia. The authors make the point that haloperidol can lead to tardive dyskinesia, but this is not mentioned as a side effect of the other psychotropics, and they describe thioridazine as "probably the most troublesome drug in the elderly." What has happened here is that the biases of the authors do not match my own.

This scholarly book has much for psychogeriatricians, geriatricians, and students in these fields. The preface states that the aim is not only to present knowledge but also to reveal our ignorance. It closes playfully with the statement, "The sooner this edition is out of date, the better." That may come to pass

in the regrettably distant future, at which time it is hoped these authors can be pressed into producing a second edition.

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SEXUALITY

Homosexuality/Heterosexuality: Concepts of Sexual Orientation, edited by David P. McWhirter, M.D., Stephanie A. Sanders, Ph.D., and June Machover Reinisch, Ph.D. New York, Oxford University Press, 1990, 423 pp., \$49.95.

Evelyn Hooker and Mary Ziemba-Davis state in their epilogue to this book that "prejudice, even among scientists, dies hard. As this volume demonstrates, however, Dr. Kinsey has at last come into a full measure of acceptance" (p. 401). *Homosexuality/Heterosexuality*, published as the second volume in the Kinsey Institute Series, is a collection of chapters written by the participants in a Kinsey Symposium convened to mark the 50th anniversary of the Kinsey 7-point scale to describe the heterosexual/homosexual continuum of behavior. The book provides an outstanding overview of current thinking in relation to sexual orientation, and its publication serves not only as a sign of the widespread acceptance of Kinsey's pioneering efforts in studying human sexuality but also as a marker of the radical changes in views of sexual orientation that have occurred since the publication of the Kinsey volumes on sexuality in men (1) and women (2).

The editors of this volume are particularly well-qualified to compile a book on sexual orientation, and they have brought together an outstanding group of authors to comment on the significance of Kinsey's work and to expand on its theoretical implications for a modern understanding of sexual orientation. As a result of the authors' breadth of expertise and the multidisciplinary focus of the text, this book provides a helpful synthesis of new information and data about sexual orientation, especially homosexuality, that should be of interest to all psychiatrists and other mental health professionals, particularly those who work in the area of sexuality.

The chapters are divided into sections that provide accounts of historical and religious, psychobiological, evolutionary, cultural and sociological, identity development, relational, and conceptual perspectives on sexual orientation. Chapters by Louis Gooren on "Biomedical Theories of Sexual Orientation," Eli Coleman on "Toward a Synthetic Understanding of Sexual Orientation," Richard Isay on "Psychoanalytic Theory and the Therapy of Gay Men," and Philip Blumstein and Pepper Schwartz on "Intimate Relationships and the Creation of Sexuality" may be of particular interest to the clinician.

Several chapters stand out in this collection of uniformly interesting selections. The overview, written by the editors, is a helpful summary of many complicated concepts related to sexual orientation and provides a succinct guide to the other chapters in the volume. The chapters by Vern Bullough, "The Kinsey Scale in Historical Perspective," and John Gagnon, "Gender Preference in Erotic Relations: The Kinsey Scale and Sexual Scripts," are clearly the products of senior and erudite scholars in the field of human sexuality who demonstrate an enormous knowledge of and fascination with their subjects. Gilbert Herdt's chapter, "Developmental Discontinuities and Sexual Orientation Across Cultures," and Letitia Anne Peplau and Susan Cochran's chapter, "A Relational Perspective on

Homosexuality," also provide clear and useful insights into their topics.

Although there are few weaknesses in this volume, it is unfortunate (and unacknowledged) that some chapters, such as those by Eli Coleman and John Money, are recycled versions of previously published articles, but even these chapters provide valuable information for the reader who is new to this field. The relative absence of specific discussions of women, except for the chapter on lesbian relationships by Margaret Nichols, reflects a larger tendency in the field to ignore the study of women's sexual orientation.

A major theme of *Homosexuality/Heterosexuality* is "a cry to elaborate the qualitative characteristics of people in a given category" (p. 401). This book is a fitting tribute to Kinsey's monumental contributions to defining the modern study of human sexuality. It responds to the cry for elaboration of the characteristics associated with men and women who have a particular sexual orientation by delving deeply into the increasingly sophisticated knowledge of the multidimensional nature of sexual desire and reminding us of the variable and unique expressions of sexuality among individuals. It further demonstrates that we can no longer use categorical and dichotomous labels such as homosexuality and heterosexuality, which are derived from a unidimensional conceptualization of sexual orientation, to describe the sexuality of groups of people.

Many of the contributors to this volume argue for a new understanding of sexual orientation that will integrate the multiple biological, psychological, and social factors shaping human sexuality and will express the complex emotional, cognitive, behavioral, and interpersonal meanings associated with sexual orientation in the lives of individual men and women. It is likely that at least some of the text for this new understanding will come from several of the authors in this volume, who demonstrate how essential Kinsey's work was in leading to our current level of understanding about human sexuality, how far we have moved beyond the work of this seminal thinker, and how much we still have to explore about this most fundamental aspect of human experience. It is a tribute to the editors and authors of this excellent compendium that the first thought that may come to the mind of the reader on completing it is, "I can't wait for the sequel to be published."

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HISTORY OF PSYCHIATRY

The American Board of Psychiatry and Neurology: The First Fifty Years, edited by Marc H. Hollender, M.D. Evanston, Ill., ABPN, 1991, 173 pp., no price listed.

The public expects a profession to demonstrate that its members have been assessed and have met certain standards of performance and expertise. The profession thus assures the public that it assesses itself in order to set and maintain stand-

ards internally rather than having them imposed by external agencies. The American Board of Psychiatry and Neurology was founded for this purpose in 1934, and the first certifying examinations took place in Philadelphia on June 7, 1935. This book recounts the history of the first half-century of the Board's deliberations, thought processes, relationships with other professional boards and organizations, etc. It is a complicated history and is well documented, providing us with the experience and deliberations of leaders in the field of psychiatry on many questions that our profession still faces, such as the relationship between psychiatry and neurology, recertification, self-assessment of practitioners, setting standards for training programs, and setting standards for practicing psychiatrists.

The book is well laid out, proceeding from the reason for the establishment of the Board through the relationship between psychiatry and neurology, the development of the examinations in both specialties, certification in subspecialties, educational "essentials" for postgraduate training, and recertification. The reasons for combining psychiatry and neurology in one board are discussed, and in his preface Dr. Hollender notes that "the problems resulting from bringing psychiatry and neurology together appeared at the very outset and were numerous and divisive" (p. ix). The gradual separation of the examination into two separate examinations is discussed. By the 1980s, Dr. Hollender notes, "Paradoxically, the divergence became greatest when scientific and clinical advances in the two specialties might have been expected to draw them closer together. The large number of psychiatry candidates and the relatively small number of neurology examiners were responsible for the logistics that promoted the separation" (p. x). The shifts and changes in the content covered by the Board examinations have reflected the many changes in the knowledge and practice of both specialties. Future decisions of the Board about the content of the examinations will undoubtedly reflect the rapidly increasing knowledge in the neurosciences, and the examinations in psychiatry and neurology may once again overlap.

Dr. Hollender's chapter on the history of the internship and S. Mouchly Small's chapter on recertification are particularly informative because the authors discuss the wide range of factors, including pressures from society and the medical professions as a whole, that influence policy decisions. The issue of recertification is clearly not resolved and will eventually have to be dealt with by the Board.

The appendixes list the directors of the Board for its first 52 years (1934–1985), a veritable Who's Who of psychiatry, and present data about the number of certificates issued each year (the data for 1956 and 1957 are missing) and the percent of candidates who passed from 1974 through 1985. I could find no reason that the percent passed was not given for all 52 years and feel it would have made the book a more complete historical document. Also, the data for diplomates in child psychiatry and neurology with special qualification in child neurology lists the number of individuals grandfathered in, but no such data are given for the diplomates in psychiatry or neurology. I was able to determine, combining data given on page 31 and in the appendixes, that 107 certificates were given the first year (1935), that 86 were grandfathered, and that 21 (68%) of 31 candidates passed.

A chapter on the research done on the different types of assessment used in past Board examinations would have contributed to the research literature on assessment. These research findings were used in making the decisions to give a written multiple choice examination as Part I, not to use es-

says, to drop some of the oral examinations, to establish training for the examiners of Part II, and to use both live patients and videotapes. These are important decisions based on sound research on assessment. Additionally, an appendix consisting of the content covered in both the written and oral examinations over the years would have been an excellent addition.

This book serves a very useful purpose as documentation of the history of an important part of our profession. It should be read by anyone who is examining or going to examine for the Board who wants an in-depth perspective of the meaning, purpose, and development of the process. The historical perspective of this book is a resource for members of our profession who are involved in setting policy about recertification, about knowledge that is required for certification, and about standards for training in postgraduate training. All residency programs should have this book in their libraries as part of the literature on the history of psychiatry.

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The Private War of Mrs. Packard, by Barbara Sapinsley. New York, Paragon House, 1991, 210 pp., \$19.95.

Barbara Sapinsley tells the story of Elizabeth Parsons Ware Packard (1816–1897), whose involuntary admission to the Illinois State Hospital for the Insane at Jacksonville at the behest of her husband, the Reverend Theophilus Packard, Jr., subsequently led her to successfully campaign for changes in civil commitment laws across the United States. Ms. Sapinsley provides us with a readable volume that, despite the author's claim, does not exactly rescue Mrs. Packard from obscurity. E.P.W. Packard has been the object of attention of Phyllis Chesler (1), Alan Dershowitz (2), and Thomas Szasz (3). Unlike these and other authors who have tackled the subject of Mrs. Packard, Ms. Sapinsley had access to Mrs. Packard's descendants and to the diaries, journals, and other documents of several generations. What more do we learn from this treatise?

We learn less than we might because Ms. Sapinsley decided not to name sources—there are no footnotes, no notes for each chapter, no list of references. The absence of sources is a problem not only for scholars who would be interested in pursuing further study but also for the general reader. One often cannot tell when statements are being made by Mrs. Packard from her nineteenth-century outlook and when observations are being made by Ms. Sapinsley from her modern perspective. In fact, much is simply paraphrased directly from Mrs. Packard's books. For example, Ms. Sapinsley writes,

The stove cleaning became a festive occasion for the fun-starved children. They insisted that "Black Prince" now shone as brightly as he had when their mother was housekeeper. After the job was done, they cleaned themselves up and then went to Elizabeth's room to warm up before retiring. Theophilus hastily gathered up his books and papers and withdrew. In his hurry, he left behind a bundle of letters which he apparently didn't miss and Elizabeth didn't notice until later.

At first she put them aside. After all, the letters were his and she had no right to pry. But then she decided that under her present circumstances, forewarned was forearmed and anything that gave her an advantage in self-protection and self-defense was legal as well as

moral. So she read them. Then, to make sure she had read aright, she read them again, and panicked.

The letters were from Dr. McFarland, Theophilus's sisters, and a Dr. Prince, head of an asylum in Northampton, Massachusetts, which did not demand curability as a condition of admission (p. 108).

Mrs. Packard's original rendition is as follows:

When our merry polishing party had completed their task to their entire satisfaction, insisting upon it that "Black Prince" looked now just as bright as he used to shine when mother was housekeeper, we cleaned ourselves and all retired to my room to warm before retiring for the night. Our entrance was the signal for Mr. Packard's leaving, of course, and in his haste or carelessness in gathering up his papers he overlooked a package of letters, which he left behind upon my table. These I did not notice until all had dispersed and Mr. Packard had locked me up for the night.

My first thought was not to examine them, as they were undoubtedly left by mistake. But upon second thought I concluded it not only right to see my husband's papers, but also to avail myself of every lawful means of self-defense which lay within my reach. Accordingly I spent several hours of this night in carefully reading these letters, received during my incarceration and since my discharge. From these replies to his own letters, his platform of action, both past, present, and future, was distinctly portrayed, bearing most fearful and unmistakable evidence that I was to be entered in a few days into Northampton Insane Asylum for life!

One of these letters from Doctor Prince, Superintendent of that Asylum, assured me of this fact. (4, p. 17).

Nor does Ms. Sapinsley differentiate Mrs. Packard's beliefs about what might happen from what history shows us might have happened. Ms. Sapinsley notes that "Dr. Prince could then lock her up for life." This view might have been appropriate for Mrs. Packard, but Ms. Sapinsley should have told us that had Mrs. Packard arrived at Northampton State Hospital, within months Dr. Prince would be dismissed due to his poor management. Pliny Earle became the superintendent, and Dr. Earle might well have agreed with Mrs. Packard that she did not require continued hospitalization and discharged her (5).

Not only does Ms. Sapinsley fail to provide a historical perspective to Mrs. Packard's treatment, she misses interesting aspects of Mrs. Packard's progenitors, despite her rich source material. For example, there was considerable turmoil between Reverend and Mrs. Packard in regard to their repeated tarnishing of each other's reputations. It is perhaps ironic, and perhaps revealing of family dynamics, that E.P.W. Packard's father-in-law had years earlier delivered a sermon on the evils of slander. Neither son nor daughter-in-law heeded his counsel:

You perceive the effect, when you look at a house, when happiness is banished, and domestic warfare reigns with all its train of miseries; here a man's foes are they of his own household . . . We remark again, that the practice of slander and raillery defeats its own object. (6, pp. 9, 14).

Ms. Sapinsley does present the reader with previously un-

published material. Noteworthy among these is a description of Mrs. Packard's admission at age 19 to Worcester State Hospital for 6 weeks and quotations from her record at that institution. One assumes that Ms. Sapinsley obtained this material from (or with the authorization of) family members, since previous researchers have been denied access to this record by the Massachusetts Department of Mental Health (7). Although not a criticism of the book per se, the question of the use of this material is an interesting one. Since E.P.W. Packard fails to mention this hospitalization in any of her books, the specter of who releases such data raises its ugly head once again. Should the record of a hospitalization of an individual who chose not to disclose this material in her own books be available on family authorization? Does it matter that the record is now 156 years old? What is the difference between this and the Anne Sexton tapes (8)?

Ms. Sapinsley provides a modern feminist perspective to the Packard story, adding commentary that is sometimes informative, sometimes intrusive. She makes remarks about what Mrs. Packard's life and mission have meant to psychiatrists, saying that she was known in the psychiatric profession largely because of the hackles she raised—and still sometimes does. Without sources, we have no way to evaluate such comments.

Ms. Sapinsley is less a historian and less an analyst than she is a storyteller. She has tough competition, however, because Mrs. Packard was herself a most skillful storyteller. But Mrs. Packard's works (and she related her history in several published versions) are not easily found. Since few will be able to read the originals, Ms. Sapinsley's version, despite its problems, should serve psychiatry well.

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PSYCHIATRIC TEXTBOOKS

Synopsis of Psychiatry: Behavioral Sciences and Clinical Psychiatry, 6th ed., by Harold I. Kaplan, M.D., and Benjamin J. Sadock, M.D. Baltimore, Williams & Wilkins, 1991, 903 pp., \$44.00.

An enticing soft cover in black with gold titles inside red-lined frames greets the reader's eye as the sixth edition of the *Synopsis* in 20 years heralds a renaissance of sorts for the "eclectic and multidisciplinary approach." In fact, the preface

is an eloquent promise to foster "the humane and compassionate aspects of medicine," so that the United States can avoid producing "computer-like, robotic physicians." Who would not wholeheartedly endorse the consideration of "the whole patient" and the study of the "sociopolitical forces that affect medical practice"? The stage is grandly set for an intellectual feat. Does the product then live up to the expectations of the consumer? I would answer by purposefully misquoting one of Spinoza's most famous statements: "I do not presume that I understand the true philosophy, I know that I have found the best philosophy" (1, p. 17).

Kaplan and Sadock envision a "teaching system" built on the durable *Comprehensive Textbook of Psychiatry*, the 5th edition of which appeared in 1989 (2). Building blocks of the system will be this *Synopsis*, a study guide, a pocket handbook, and a comprehensive glossary of psychiatric and psychological terms. The assistance of the venerable American Board of Psychiatry and Neurology and the National Board of Medical Examiners helps this volume to reach a worldwide readership. The text has been translated by now into five foreign languages. Without a doubt the vision is imposing, the landmarks glowing, the road very inviting. Thus we must enter into the foundation building.

The structure is made out of 48 chapters, the first one most appropriately titled "The Doctor-Patient Relationship" but conceptualized essentially as the typical psychiatric interview. The flow of chapters is good, but one wonders why the book was not divided into six obvious sections: basic sciences, clinical examination, adult clinical psychiatry, treatment approaches, child and adolescent psychiatry, and special areas such as geriatrics, forensics, ethics, and the history of psychiatry. Well-advertised and well-executed major changes and innovations are introduced in areas such as biological therapies, brain and behavior, the life cycle, geriatric psychiatry, AIDS, and nosology and diagnosis. I particularly liked an excellent comparative table of contributions to the life cycle study, beautiful figures and illustrations in the chapter on brain and behavior, useful comparisons of psychometric and neuropsychological tests, and a thorough list of the main psychiatric rating scales. From a clinical perspective, the discussion of temporal lobe epilepsy psychosis is an excellent piece, as are the chapters on AIDS, psychoactive-substance-induced mental disorders, and substance use disorders. Chapters on recent clinical observations such as the coexistence of anxiety and depression and chapters on sleep disorders, factitious disorders, impulse control, and adjustment disorders live up to their billing. The text on biological therapies is particularly strong and very well done. The same is true for the chapters on mental retardation, developmental disorders, anxiety disorders of childhood and adolescence, gender identity, and other disorders of infancy, childhood, and adolescence. I found the sections on special areas of child psychiatry (mood disorders and child abuse) and the chapter on psychiatric treatment of children and adolescents quite well-written and instructive. The same goes for the sections on forensic psychiatry and psychiatric ethics. The psychotherapeutic drug identification guide, which contains full-color illustrations of all the major drugs used in psychiatry in various dosage forms, is simply captivating, even though it could have been better placed in the psychopharmacology chapter.

So, is there something wrong with this sixth edition? The answer is almost a whisper: "No, but." What makes it a little less than a resounding success could be seen, from a different perspective, as the main strengths of the volume, namely, its appeal to different levels of readers and its all-encompassing, clear-cut, precise outlining of the different and complex areas

of our precious discipline. In doing that, the *Synopsis* smacks, at times, of vagueness and overgeneralization, omits some precise data, and gives the false impression of thoroughness and ultimateness, with self-contained units that do not even have adequate cross-references. Thus, it leaves little room for dissension, doubts, and ambiguity, so central to the contributions of authors such as Jerome Frank, van Praag, Kuhn, and Torrey. It creates what Schoolman (3) would call a "coercion for conformity . . . [that will] destroy the essential environment of fostering controversy, welcoming iconoclasm and providing refuge and a forum for rebels" (p. 89). In short, I missed a chapter on current controversies in psychiatry. An eloquent example of this is the omission of names such as Anna Freud, René Spitz, Karl Jaspers, and Kurt Schneider from the dry chronological history of the last chapter (my biggest disappointment). In spite of proclaiming that events are more important than individuals, only 15 events are listed in this chronology of 123 items. In addition, a pervasive blank in the promised "wholistic" approach is the role of social and cultural factors in psychiatric theory, psychopathology, research, and education. There is not much about the "sociopolitical forces" at play in the practice of psychiatry either, and the view of the whole discipline is inevitably tinged by the Northern Hemisphere-Western-Anglo-American view of the world, psychiatric and otherwise. I guess the *Synopsis*, like many other American books, cannot quite solve the dilemmas of whom to address the product to and how to package it. Although attempting to reach the whole world (as indeed it will, and justifiably so), the book cannot shake off an essentially American flavor.

Errors, omissions, and incomplete and ambiguous data appear here and there as little specks on an otherwise harmonious canvas. The International Pilot Study of Schizophrenia did not include Hutterites, Croats, or Tongans; some clinicians would disagree with the definition of dysphoria as merely "an unpleasant mood"; Hamilton's paper on assessment of anxiety states is said to have been published in a nonexistent British journal; tuberculosis is not a viral infection; and using interpretative psychotherapy in rheumatoid arthritis sounds as wrong as misspelling "geophagia" twice.

To devote only two paragraphs to the *International Classification of Diseases* betrays the purpose of updating the nosological advancements in the field. Jaspers and Kretschmer are not mentioned in the chapter on schizophrenia, and the Tsuang-Winokur criteria are also omitted. The list of culture-bound syndromes is obviously incomplete. Cushing's disease, hyperparathyroidism, and liver transplant are not mentioned in the chapter on psychosomatic disorders. Another gross omission is the lack of mention of cultural and social factors in the development of personality disorders. A table of the main brief psychotherapies and a listing of drug-drug interactions would have been helpful.

The discussion of dysthymia is incomplete because no mention is made of its close connection to borderline personality disorder; the assessment of obsessive-compulsive disorder and its treatment does not include neuropsychological testing or the use of augmenters. Many will frown when reading that psychotherapy is useful for delusional disorder and that insight-oriented psychotherapy is advocated for paraphilias, some of which are clearly associated with psychosis. Likewise, one is not sure whether depersonalization is a symptom or a syndrome, even though we know that it can be both. Finally, when supportive psychotherapy is considered a form of psychoanalytically oriented psychotherapy, our doubts threaten to become almost unsurmountable.

There are soothing passages, however. It is nice to see nine

pictures of Freud and his life, no matter how a lot or a little biased that may appear. It is a different kind of bias to equate anxiety with autonomic neuroendocrine reactivity, but to see the end of the psychoanalytical emphasis on anorexia nervosa is reassuring. Somebody may think that mixing vignettes with study series may be forgivable, but not when the standard warning about the simultaneous use of monoamine oxidase inhibitors and tricyclic antidepressants is omitted, or when a table of differential diagnosis in psychiatric emergencies and a picture of a brain with Alzheimer's disease are duplicated.

Enough for the picky evaluation of a book that, although imperfect like psychiatry itself, is full of excellent pages. Some people may even say that the purpose of this volume is not what this review seems to demand. Still, if somebody asks me whether I would choose this book to find useful information, the answer is a resounding yes. The book does justice to what Dr. Nemiah would tell us about the vastness and the richness of this discipline of ours (4). If the *Synopsis* does not have the answer we are looking for, there is always the *Comprehensive Textbook of Psychiatry*, or the intangible wisdom of our own patients, always ready to lead us out of our uncertainties and our ignorance.

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Principles of the Psychiatric Evaluation, by Roger A. MacKinnon, M.D., and Stuart C. Yudofsky, M.D. Philadelphia, J.B. Lippincott Co., 309 pp., \$29.95 (paper).

This book is the retitled but largely unchanged revised edition of Drs. MacKinnon and Yudofsky's 1986 work, *The Psychiatric Evaluation in Clinical Practice*. This updated edition builds on the strengths of the original; it is at once comprehensive yet succinct, opinionated yet not doctrinaire. Drs. MacKinnon and Yudofsky are noted individually for their work in the fields of psychoanalysis and neuropsychiatry, respectively, and their collaboration here manages to be integrative where other comparable textbooks are limited; therein lies this book's particular value.

Chapters 1 and 2 are devoted to the psychiatric interview and the clinical examination of the patient. The discussion of the psychiatric interview includes nuts and bolts observations—about seating arrangements and note taking, for example—as well as more theoretical concerns such as transference and countertransference phenomena in a first meeting. The chapter on the clinical examination focuses on the psychiatric history and the mental status examination and includes an extensive inventory developed for the written history that should be useful for beginning residents, given its wide scope. Complementing the review of the mental status examination

is a discussion of two examples that underscore common pitfalls in its execution and interpretation.

Chapter 3 is an ambitious attempt to catalog the wide range of biological tests now available to psychiatrists. Familiar topics included are neuroendocrine assays, brain imaging techniques, and electroencephalogram diagnosis. The review of pharmacotherapy briefly addresses critical points in the initiation and monitoring of treatment with better-known medications as well as newer ones such as clozapine. Finally, the authors have added to this edition a timely set of guidelines to use in consideration of testing for HIV.

Chapter 4 focuses on the localization of brain function as well as psychopathology associated with diffuse cortical impairment, and chapter 5 lists a number of psychological tests and psychiatric rating scales. Some of the frequently used intelligence evaluators, personality tests, and neuropsychological batteries are outlined, among them the WAIS-R, WISC-R, Rorschach, Thematic Apperception Test, MMPI, and Halstead-Reitan. In the chapter appendix, seven psychiatric rating scales are reproduced, including the Beck Depression Inventory and the Hamilton Rating Scale for Anxiety. Given their wide use as research tools, it makes sense to include such familiar scales.

The sixth and last chapter is devoted to *DSM-III-R* diagnosis and psychodynamic case formulation. An extensive consideration of the written psychodynamic case formulation follows a brief review of the multiaxial evaluation according to *DSM-III-R*. This examination of key psychodynamic topics (ego functions, Freud's tripartite model, a scheme for symptom formation) ought to be easily understood by a beginning resident in the throws of his or her first case formulation. Three complete examples of case formulations follow this discussion.

Any text attempting to cover all of modern psychiatry in slightly more than 300 pages will be plagued by omissions; in this case some, like the dearth of information on tardive dyskinesia, are more glaring than others. The authors, however, take into account the inherent shortcomings of so broad a project by providing extensive bibliographies after each chapter. The breadth of material covered makes this volume indispensable for the trainee building a collection of references. Its wide scope also highly recommends the book to nonpsychiatrists interested in the current trends in psychiatric treatment. The particular value to psychiatry trainees of this and similar texts that stand resolute in their efforts to synthesize the biological and the psychodynamic cannot be overestimated.

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RELIGION

The Divine Archetype: The Sociobiology and Psychology of Religion, by Brant Wenegrat. Lexington, Mass., Lexington Books (D.C. Heath and Co.), 1990, 207 pp., \$29.95.

For many, sociobiology is not of great interest; most of the standard psychiatric textbooks do not discuss it. However, to its adherents it is essential to understanding how humans behave. Sociobiologists study social behaviors of animals on the assumption that human behaviors have evolved from lower forms of life by means of evolution over the millennia.

This book arranges a marriage of psychoanalytic and neo-Darwinian theory to explain the origins of the religions of mankind. The author concludes that just as species-specific

animal behaviors have evolved which enhance adaptation of the species, so has mankind evolved religious beliefs to help members of our species sort out their sexual conflicts, promote cooperation, and encourage altruism.

If one wants to find out about sociobiology, this is an excellent place to start. There is a chapter that summarizes much of what sociobiologists talk about. There are 500 references in the bibliography. There is an interesting appendix, with summaries of numerous published case histories in which religious preoccupations were mixed in with serious psychopathology.

I was disappointed with the author's analysis of religions, which I found to be reliant on oversimplifications and psychological reductionism. For example, he says that "religious persons tend to be obedient, conforming, and anxious to obtain external approval" and that "believers most attracted to prayers like the 23rd Psalm are those with the greatest dependency needs."

The author misstates the conclusions of one of his citations defending his contention that certain yeshivas (Jewish seminaries) are "ultraorthodox cults" like the Unification Church and Scientology. The actual citation (1) concluded that crucial differences distinguish cults and yeshivas.

Although the author gives credit where it is due (noting that religious organizations set up soup kitchens and hospitals) and does not give all religions hard knocks (he is particularly positive about Islam), he clearly takes a wary view of religion. He suggests we come to terms with Freud's failed prophecy that religion will disappear and hopes that religions will be modified so that they can keep up the good work with "less personal cost to religious believers."

The author is troubled by the history of religious opposition to neo-Darwinism. He cites the "ominous fact" that although religion is a "great Hydra," science is a "new and possibly fragile bloom" and warns rationalists to "take note." However, neo-Darwinism has been criticized on statistical grounds by some mathematicians (2), without benefit of any theology.

The book's postulates are that 1) the psychoanalytic theory of Freud and Jung accurately describes the human condition, 2) the neo-Darwinian theory of random evolution is true, and 3) the religions of the world are complex creations of man's imagination. The number of these postulates that a reader accepts or rejects will determine whether he or she finds the book of great interest, of no interest, or somewhere in the middle.

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FEAR, ANXIETY, AND COURAGE

Fear and Courage, 2nd ed., by S.J. Rachman. New York, W.H. Freeman and Co., 1990, 393 pp., \$32.95; \$17.95 (paper).

When contemplating fear and courage, I recall a tidy biographical illustration. As a small boy, Ernest Hemingway

shouted, "Fraid o' nothing," and these words, linked to his father's expectations, guided him long after he knew better (1). He was wounded as a young man fighting in Italy during World War I, and throughout his life he chased wars and danger as willingly as he chased women. He acted fearlessly even when he knew there were plenty of legitimate reasons to be afraid. Characteristically, Hemingway held a tight rein on his fears while ardently embracing courage. He valued physical courage and endurance and imposed this code on himself until, at the end, overwhelmed by alcoholism and psychotic depression, he could no longer endure and deemed it was time to die. It would be hard to imagine that Hemingway, like many others who have struggled with the contending faces of fear and courage, would not find some pithy commentary in the revised edition of *Fear and Courage*.

Not surprisingly, the bulk of this book centers on the subject of fear rather than courage. This is not unusual when we consider that the more unsettling emotions and behaviors predominate in the pages of psychiatric journals and textbooks. Even our clinical observations seldom emphasize our patients' emotional or physical strengths. It is precisely Rachman's different stance when looking at fear, fearlessness, and courage that distinguishes this book from other more traditional texts on fear and anxiety. He feels that the psychological literature on fear exaggerates human vulnerabilities at the expense of celebrating man's limitless capacity for adaptivity and acts of noble quality.

The book is divided into six sections—Fears in War, Varieties of Fear, The Acquisition of Fear, The Modification of Fear, Courage, and Conclusion. Even though the topic of courage formally occupies only a brief and final piece of this work, the themes of fearlessness and courage are interwoven throughout the text. The tone is optimistic, and since its previous edition in 1978, roughly half of the material is new and focuses on the author's broadening interests in courage, the overestimation of fear, methods of fear reduction, and the nature of panic. Original research is also described.

The book opens with a section discussing fears in war and emphasizes the unexpected emotional adaptivity of civilian populations to withstand enemy air attack. It seems that in the early days of World War II, British civilians quickly adapted and, as painlessly as possible, accommodated their daily routine to the unrelenting air attacks that came to be called the Battle of Britain. Londoners rapidly habituated to the blitz, and with a distinctly British flare for the understatement, newspaper obituaries euphemistically read, "died very suddenly."

On the morning of August 6, 1945, in an act of war without precedent, Hiroshima was instantaneously incinerated into a nuclear wasteland. Incredibly, however, the adverse psychological effects recorded among the survivors were astonishingly small, given the sweep of the devastation. Psychosis, traumatic neuroses, and other severe psychiatric disorders were reportedly rare. Within 3 months the population returned to about 140,000. (Hiroshima's population before the atomic blast was more than 300,000.)

Throughout World War II, despite steadily more fearsome raids, the urban civilians of England, Germany, and Japan became more emotionally resilient to air attack than the less threatened rural population. Among some survivors, however, fears changed to apathetic depression as they succumbed to the uncontrollability of their plight. Fearlessness seemed to hinge on the perception of control, and this was supported by the observation that fighter pilots consistently reported less fear and had fewer psychological breakdowns than bomber pilots and crews. Seemingly, their technical knowledge, self-

confidence, and sole control of their aircraft did much to lessen their fear even when confronting the catastrophically high casualty rates of their calling. This was a time when fears were not always proportional to the gravity of danger.

Anxieties and fears are defined differently, but the feelings certainly overlap. In the section entitled *Varieties of Fear*, Rachman sheds light on a puzzling array of fears and anxieties. He recognizes that fears have boundaries and often change with age and familiarity. Fear may even be simply the fear of one's own reactions; as in panic, the mind misinterprets bodily sensations. The theme of fear intertwining with anxiety disorders is further pursued in the sections *The Acquisition of Fear* and *The Modification of Fear*. The author deftly addresses the associations between agoraphobia and claustrophobia and their shared fear of entrapment. He details the limitations of conditioning theory and recommends a revised view while offering still other pathways to the acquisition of fear: vicarious experiences and the impact of threatening information. For instance, children observing frightened adults often develop similar fears. This phenomenon was observed by Anna Freud, who founded a wartime nursery in Britain and noticed that children's fears were more related to their mothers' responses to air attack than the actual bombing. Fear, like courage, can be contagious. Depending on the intent, information can generate fear or quell fear by buoying confidence. During the recent Gulf War, the Iraqi threat of chemical warfare instilled fear, but this fear was controlled by education and effective training that demonstrated survival in a chemical environment. As the author reemphasizes when discussing systematic desensitization, fears can be unlearned; generally, circumscribed fears are quickly modified or eliminated. The therapy (training) is straightforward. But what if anxiety persists long after the fearful event passes? When the signs of this spawned anxiety become intrusive, with nightmares, obsessive ruminations, and flashbacks, Rachman suggests that a fragment of the traumatizing fear remains unintegrated. He discusses this dissociation and its treatment in the chapter called "Emotional Processing."

The strength of this work is the portrayal of new findings and ideas as well as the fresh way the author views established information. The book is quite readable, the information valuable, and the price fair. However, for readers interested in the symbolism of fear and psychoanalytic clarification, this would be a disappointing read. There is a short chapter on the psychoanalytic explanations of fear with a cutting skeptical stance regarding some of the more fanciful analytical interpretations of fears and phobias. (One wonders if the author wrote this chapter tongue-in-cheek, particularly considering his views on the classical interpretations of spider and snake phobias.) This section would have been improved with a broader introduction to the author's thoughts on psychodynamic theory and the collective unconscious.

For readers interested in fearlessness and courage who relish the psychological bend, this book is an excellent starting point. Instead of lengthy commentaries on military applications or philosophical ideals, the thrust of Rachman's discussion is on training people to perform courageously, decreasing subjective fear, and reporting original research. More than likely, some readers will have a broader and more in-depth interest in bravery, and for them, *The Anatomy of Courage* (2), written by Lord Moran, a World War I battalion medical officer who later became Winston Churchill's personal physician, is the seminal work on men at war struggling against fear.

"Courage" is a word derived from the Latin *cor*, meaning "heart." It speaks to the spirit, and terms like lionhearted and

stout-hearted are synonyms for bravery. Socrates called courage a "very noble quality," and his pupil Plato ranked it with wisdom, temperance, and justice as among the cardinal components of virtue. Aristotle, not given to extremes, valued courage, placing it between cowardice and rashness (fearlessness). The emotions and behavior that range between cowardice and fearlessness are freshly examined in this book. Rachman emphasizes how competence and self-confidence can be enhanced and eventually lead to courageous actions and increased fearlessness. He contends that even the "fainthearted" are not precluded from courageous acts. He recognizes that courage, unlike fear, is a neglected topic among mental health professionals and seems to be the subject of serious discussion only among soldiers and philosophers. ("Military biographers tend to mark physical courage as the one human trait whose absence causes soldiers to fail; in few other professions is physical courage such a mandatory qualification" [3].)

Much of courage is perseverance, and Rachman is wise to embrace the continuum between fear and courage in a single text. Similarly, as Hemingway grew, he shed the phrase "Fraid o' nothing," replacing it with the quieter courage of "Il faut d'abord durer."

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NEUROPHARMACOLOGY

The Neuropharmacological Basis of Reward, edited by Jeffrey M. Liebman and Steven J. Cooper. New York, Clarendon Press (Oxford University Press), 1989, 424 pp., \$75.00.

In principle, behavioral problems like drug addiction and alcoholism as well as other conditions such as eating disorders, sexual promiscuity, depression, and autism could be at least partly secondary to impaired brain reward mechanisms. Although animal models of human psychopathology seem to provide some support for this hypothesis, it is difficult to clearly demonstrate it because 1) mental disorders are more complex in humans than animal models can show, 2) reward systems in humans are poorly localized and recognized, and 3) "reinforcers" in humans are more complicated in nature (environmental, psychological) and quality (personality, social adjustment). This book is not designed to solve these problems but is devoted to answering basic neurophysiological, neuroanatomical, and neurochemical questions regarding reward mechanisms.

In the introductory first chapter, Jeffrey Liebman discusses the concept of reward and the main goals of the book:

Reinforcement shapes the interaction of higher animals, including humans, with their environment . . . Without reinforcement, the infant will not learn about the significance of other humans, the child will not heed warnings of danger . . . Reinforcement may take place

through the presentation of an appetitive stimulus or the removal of an aversive stimulus. The former instance is termed positive reinforcement and the latter negative reinforcement. This volume is concerned exclusively with the first of these instances, in which an appetitive, positive reinforcer increases the likelihood of subsequent responding. This contingency is commonly considered as an instance of reward.

In chapter 2, "Pharmacological Basis of Intracranial Self-Stimulation Reward," James Stellar and Mathew Rice deal with crucial methodological aspects of intracranial self-stimulation reward (like behavioral measurement and reward specificity) and then discuss the effects at the level of different neurotransmitter and neuromodulatory systems. A large body of evidence seems to indicate that dopaminergic systems are related to the reward produced by stimulation in the medial forebrain bundle. Stellar and Rice conclude that "whatever the exact nature of accumbens . . . [dopaminergic] functions and how they interact with reward, the importance of the accumbens to self-stimulation behavior of the medial forebrain bundle seems clear."

A further contribution to this topic comes from chapter 3, "Neuroanatomical Bases of Intracranial Self-Stimulation: Untangling the Gordian Knot." Here Anthony Phillips and Hans Fibiger discuss the complexity of demonstrating brain stimulation reward phenomena experimentally and point out the need to consider them as "subserved by many different regions of the brain rather than a unitary system located within the medial forebrain bundle."

Chapter 4, "Neuronal Bases of Intracranial Self-Stimulation" by Peter Shizgal and Beverley Murray, deals mostly with the "methods for distinguishing the directly stimulated neurons responsible for brain stimulation reward from the many other neurons that may be concurrently activated by the electrode."

In chapter 5, "Drugs as Reinforcers: Pharmacological and Behavioural Factors," Jonathan Katz reviews the literature on the reinforcing effect of different drugs such as opioids, cocaine, amphetamine, and their antagonists. Data on the possible mediating effects of dopaminergic pathways on the reinforcement by opioids are controversial: opioids could act through kappa, delta, or sigma receptors. Katz points out that the potency of dissociative anesthetics such as phencyclidine as reinforcers is closely related to their potency in displacing [³H]phencyclidine from brain membranes. He says that "there is no evidence to support the hypothesis regarding a final common dopaminergic mediation of the reinforcing effects of all abused drugs."

Chapter 6, "Neuroanatomical Substrates of Drug Self-Administration" by George Koob and Nick Goeders, deals with intravenous and intracranial self-administration of drugs. More than 20 psychotropic compounds that are self-administered by humans have been found to act as reinforcers in rats, suggesting that drug self-administration in animals may be a reliable predictor of human abuse. Of particular interest are the data showing that lesions in the nucleus accumbens can markedly decrease cocaine and amphetamine self-administration in rats. In general, the dopaminergic system seems important for indirect sympathomimetic self-administration, but systems other than the mesolimbic-mesocortical dopaminergic structures, perhaps the glutamatergic, could play a role in opioid self-administration.

In chapter 7, "Conditioned Place Preference as a Measure

of Drug Reward," Geoffrey Carr, Hans Fibiger, and Anthony Phillips show that data based on the conditioned place preference paradigm are not comparable because of different methodologies; therefore, it is impossible to draw any sound conclusions. These authors stress the need for standardization of procedures.

In chapter 8, "Central Neurotransmitter Systems and the Control of Operant Behaviour by 'Natural' Positive Reinforcers" by C.M. Bradshaw and E. Szabadi, studies involving not only catecholaminergic but also cholinergic and peptidergic pathways for the effective regulation of operant behavior by reinforcers are reported, but a satisfactory paradigm integrating these pathways in the general reinforcement paradigm is not available.

In the final chapter, "The Brain and Reward" Roy Wise states that we do not know if the unitary or multiple neural/neurochemical mechanism theory is more adequate to explain reinforcement phenomena; however, there are important proofs for the role of dopaminergic pathways (particularly of the nucleus accumbens), although other systems seem to be involved. Common physiological mechanisms could underlie all these behavioral phenomena, but there is also the possibility that "each phenomenon is independent without sharing a common final pathway in the brain."

This is a high-quality book, rich in information (sometimes controversial or overlapping) not readily available to clinicians because it is primarily directed toward basic scientists. From a clinical point of view, the biological concept of reward, although highly fascinating, is still in some way speculative, and any effort to extrapolate data from the laboratory to normal and pathological human behavior seems premature.

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DREAMS

The Manifest Dream and Its Use in Therapy, by Roy M. Mendelsohn, M.D. Northvale, N.J., Jason Aronson, 1990, 256 pp., \$35.00.

In *The Interpretation of Dreams* (1), Freud took pains to distinguish the manifest from the latent content of the dream. Emphasizing his fundamental mistrust of the manifest content, he likened manifest content to the facade of an Italian church that bore no relation to the structure inside. He did so in order to argue for the point of view that the dream has a structure similar to that of the psychoneurosis and can be analyzed by using the method of association of ideas into latent content disguised by the dream work. Freud took great pains to assert that dreams should be analyzed in this way rather than being interpreted on the manifest level as allegories, symbols, or parables.

Part of this legacy of Freud's original investigations on his own and his patient's dreams has been what many analysts today would consider an excessive rejection of the manifest content of the dream as clinically useful. Not the least of the difficulties resulting from this point of view is that the dream becomes virtually unclassifiable. Federn (2) pointed to the usefulness of ego feelings in the manifest dream. In a seminal paper written in 1954, Erikson (3) pointed the way to a more balanced view of the manifest content in relation to the latent content and affirmed the overall usefulness of the manifest

dream. Since then, a good deal of clinical and empirical attention has been given to the manifest content in relation to diagnosis, in relation to clinical predicament, and in the context of the clinical course of the analysis or therapy. Although there is generally consensus that the manifest content has value, especially in conjunction with associative material and awareness of process, rather little has been written on the manifest content in relation to the process of psychoanalysis or psychotherapy.

Roy Mendelsohn's book is a big step forward in that direction. Mendelsohn has a nuanced and synthetic view of psychopathology, seeing the manifest dream as indicative of the state of cohesion of the self in relation to the type of object relationship needed to face conflicts at the libidinal and developmental level at which patients find themselves. This takes place in the context of the therapeutic or analytic process. That is to say, the day residue has very much to do with the treatment situation and the patient's unconscious perception of the therapist or analyst. Mendelsohn's many-faceted grasp of psychopathology seems to me the centerpiece of his bold attempt to argue for the value of the manifest dream in the context of the therapeutic process. Although current dynamic thinking has headed unequivocally toward considering the dream in the context of the process, Mendelsohn's awareness of processes of fragmentation and reconstitution of self-experience in relation to an object for the entire spectrum of psychopathology is both brilliant and unique.

The book, however, is not without difficulties. I found it hard to read. It is thick with theory and sometimes with idiosyncratic terminology. I found many of the numerous examples of the interpretation of the manifest dream debatable or outright unconvincing, and when I turned from the conclusion being drawn to the actual evidence supporting it, I felt sorely in need of associations to settle the matter. I am not convinced by the clinical material put forward that manifest dream material is in as close correspondence to overall psychopathology as Mendelsohn implies. He leaves the impression that the dreams of schizophrenic patients are always revelatory of schizophrenic psychopathological predicaments, the dreams of borderline patients are always revelatory of borderline psychopathological predicaments, and so forth. The bulk of the literature on the subject so far disputes this, and Mendelsohn's overriding assumption that the manifest dream is always indicative of specific psychopathology seems to me not at all substantiated by the evidence.

Despite these shortcomings, I see this as an important, bold, at times brilliant, synthesizing book that any serious student of dreams from a psychodynamic or psychoanalytic perspective will want to read.

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DEPRESSION

Refractory Depression, edited by Jay D. Amsterdam. New York, Raven Press, 1991, 249 pp., \$60.00.

The pharmacotherapy and electrotherapy of major depression have had many successes and some failures. For most patients, these therapies shorten the length of individual episodes of depression or prevent or delay relapse and thus change the course of their illness. Unfortunately, a subset of patients with mood disorders develops chronic depression. Intriguingly, the proportion of depressed patients who develop refractory symptoms may not have changed since Kraepelin established that approximately 20% of his patients did not spontaneously improve. Refractory cases have become an important part of the caseload of psychiatrists because patients with straightforward depression are increasingly being treated by internists or family practitioners and only treatment-resistant cases are referred on to psychiatrists.

Refractory Depression is a collection of chapters written by many of the established experts in treating refractory or treatment-resistant depression. It meets the need for a comprehensive, in-depth compendium of data and views on the topic. The first chapter reviews the difficulties inherent in defining adequacy of a single trial and in defining treatment-resistant depression. It endorses Schatzberg's proposed model of quantifying both severity and lack of treatment response. Its most useful contribution is in citing the limitations of many existing studies. Several chapters review the hypothesized pathophysiology of affective disorder. There is some overlap among these chapters, but this is outweighed by the intriguing discussions of interactions among the various neurotransmitter and receptor systems. Clearly, no single theory has been able to integrate the existing pharmacological, neuropathological, biological marker, and imaging studies into a coherent model. It seems most likely that new discoveries will need to be made before specific pathophysiologies of the affective disorders are found.

The chapters reviewing specific therapeutic maneuvers will be of most interest to clinicians. The book has helpful reviews of lithium augmentation, carbamazepine, thyroid augmentation, stimulants, and combinations of monoamine oxidase inhibitors and tricyclic antidepressants. Also reviewed are the use of estrogen (one placebo-controlled study) and spironolactone and pemoline (no control studies for either). A chapter on depression in childhood emphasizes our lack of knowledge about the diagnosis and treatment of affective disorders in children and the need for much more research in this area. A review of stimulant drug use in the elderly will be of interest to researchers and clinicians alike. Of note in these chapters is the clear identification of areas in which knowledge is lacking and of weaknesses in existing studies.

A chapter summarizing the many clinical studies would have made a nice addition to this excellent volume. Unfortunately, there are so few studies comparing different treatment regimens that little guidance can be given to the clinician facing the thorny problem of choosing among the available treatment options.

Reprints of Book Forum reviews are not available.

Letters to the Editor

EDITOR'S NOTE: We present herewith a representative selection of the many Letters to the Editor commenting on the article about psychotherapist-patient sexual contact by Dr. Paul Appelbaum and Ms. Linda Jorgenson—a response that is by far the most vigorous and extensive the Journal has seen in many years. The authors' rejoinder to their correspondents and the related editorial by Dr. Jeremy Lazarus published elsewhere in this issue speak directly to the ethical problems that are at the center of the controversy. We should, however, like to comment briefly here on the question concerning editorial policy raised in two or three of the letters that follow.

The Editor is the doorman, not the turnkey of the Journal's gates; his task is to facilitate the admissions to its pages of papers dealing with the wide spectrum of topics and opinions that reflect the variegated interests of its readers. The constraints of space, of course, force him to make choices from among the many manuscripts submitted for possible publication, but his selection of what eventually appears in print is not influenced by pressure from those who would rather burn than broadcast ideas unpalatable to them, nor is it determined by the dictates of APA policy. Indeed, the trustees, officers, and directors of the Association have invariably been sedulous in allowing him editorial autonomy, without which the Journal would lack academic and scientific credibility. Excellence—scientific, intellectual, literary—and appropriateness for the general readership of the Journal are the primary criteria for the acceptance of manuscripts for publication, and in making his selections, however innately wrongheaded his editorial judgment, the Editor is restrained from recklessness by the wisdom and advice of the multitude of colleagues who so generously answer his requests for peer review.

The paper by Dr. Appelbaum and Ms. Jorgenson is no exception. Well versed in the practical and theoretical aspects of medical ethics, its referees praised the manuscript for the clarity of its writing and the rigor of its arguments, and despite disagreement with its basic ethical conclusions, strongly recommended its publication as a vital contribution to an important and topical professional debate—refreshing advice in an era of political correctness.

J.C.N.

Psychotherapist-Patient Sexual Contact After Termination of Treatment

SIR: While applauding the focus given to the topic of posttermination romantic and sexual relationships between therapists and their former patients by the publication of the article by Paul S. Appelbaum, M.D., and Linda Jorgenson, J.D. (1), we disagree strongly with both their conceptualization of the problem and their proposed remedies. We believe that such remedies, presented in the name of a practical solution, would, if adopted, expose patients to unnecessary risks of harm. The signatories of this letter all have extensive experience in the field of patient-therapist sexual relationships as researchers, expert evaluators and witnesses, and/or treating therapists, and these various perspectives inform our response to this article. Several of us are

distressed to find isolated portions of our own published work cited to support inferences which we believe to be mistaken and which do not reflect our writings when taken as a whole.

We disagree with the notion that such posttermination relationships simply represent one variation upon the theme of consensual sexual relationships between adults. Apart from the in-court statements of those therapists who engage in such activities, we are aware of no professional literature, either theoretical or empirical, which would support such a construction of these relationships as consensual and probably no worse than other tolerably problematic relationships between adults. Such a statement ignores what is known about the enduring effects of both transferential and nontransferential aspects of therapy, which have been demonstrated to persist for as long as a decade after termination (2–8). There are no research studies available that would support a contention that any such relationship begun more than 1 year after termination would not entail risks of harm to patients.

We also challenge the conclusion that a 1-year waiting period would be a sufficient rein on such relationships and would serve to prevent most foreseeable harm. Dr. Appelbaum and Ms. Jorgenson cited data, essentially drawn from studies that did not have posttermination relationships as their primary focus (2, 3), that seem to indicate that a majority of such relationships reported in these studies became overtly or genitally sexual within 6 months of the official termination of therapy. They interpreted this to mean that these relationships were the result of a "hasty infatuation" on the part of the therapist and/or patient that would fade over time if a 1-year waiting period were put into place as they suggested. They suggested that a 1-year ban would be practical, since it provides a clear time period to a therapist wishing to propose such a relationship, and at the same time would purport to protect patients by giving them time to consider.

Our experience indicates otherwise. This brief latency between official termination and initiation of overt sexual relationships is indicative of the nonconsensual, transferential nature of the relationship.

Dr. Appelbaum and Ms. Jorgenson disregarded the risks present in offering to either therapist or patient an official time at which overt sexual contact may commence (4–7, 9, 10). When the possibility of a sexual relationship exists in the mind of either party, but particularly that of the therapist, psychotherapy can and all too often *does* become a courtship, a process of grooming in which a vulnerable individual is shaped to meet the sexual and narcissistic needs of the therapist. Therapy in such a case ceases to be in the interest of the patient's growth and may take paths which are antithetical to her or his well-being when the goal of becoming a sexual or romantic partner of the therapist becomes a predominant one.

If this grooming, which is inevitably countertherapeutic, includes the imposition of a 1-year waiting period, we fail to see how this prevents harm or avoids the intrusion of the therapist's sexual and narcissistic needs into the field of psychotherapy. A 1-year posttermination rule for sexual relationships between therapist and patient may lead to more premature terminations of treatment; it may make the relationship more

valued, and less questioned and reflected upon, because of the obstacles of time and separation placed upon it. We are all aware of cognitive dissonance theory which suggests that the higher the price, the more valued the choice and the less likely that it will be critically reflected upon. Dr. Appelbaum and Ms. Jorgenson err in suggesting that our professions reward those individuals with better impulse control and ability to delay gratification and ignore the meaning of their activities.

Dr. Appelbaum and Ms. Jorgenson emphasized that few appellate cases involving posttermination sex have been reported, implying that this may be much ado about nothing. However, the number of appellate cases may be an unreliable, biased, and unrepresentative guide to the relative frequency of either the number of civil cases filed in the instance of a posttermination relationship or the number of such relationships per se. In fact, in our collective experiences, such cases are becoming one of the common varieties of sex between therapist and patient (4, 10). Many cases are settled before trial and thus would not be appealed. Most cases never enter the complaint process at all.

Dr. Appelbaum and Ms. Jorgenson also argued that there is no strong evidence for harm as a result of such relationships. While we would agree that the published literature is short on such information, and consider ourselves partly responsible for not having collected and published the information we have gathered in the course of our clinical work, our impressions are otherwise. That is, we have seen the same type and severity of harm devolving from posttermination relationships as from those initiated by therapists with less effective impulse control (10). The one available empirical study (4) does indicate that subsequent therapists were able to identify evidence of harm to clients in approximately 80% of such cases of posttermination relationships; this cannot be seen as an insignificant number. There is also no evidence at all to suggest that posttermination relationships, whenever they commence, do not cause harm.

We do not believe that it is justified, clinically or ethically, for a therapist to engage in sexual intimacy with a patient or former patient, regardless of the amount of time that has elapsed between termination and the sexual intimacy. However practical a 1-year rule might be, it would be improper to allow questions of practicality to override those of ethics and concern for the welfare of vulnerable individuals. There is no reason why therapists should take such risks with the well-being of anyone whom they have encountered in the course of a doctor/therapist-patient relationship given the magnitude of the harm that can and often does occur. To establish an arbitrary 1-year waiting period ignores the dynamics of the therapeutic relationship and the long-lasting effects of those dynamics, while it carries the implicit message that such relationships are permissible. This will encourage abuses which can only create added risks of harm for patients.

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SIR: As a victim of sexual misconduct by a physician/therapist, I read with great interest the article by Dr. Appelbaum and Ms. Jorgenson.

From my association with other victims and experience with caring mental health care professionals, I have heard a resounding "It's never OK" to have a romantic/sexual relationship after therapy is terminated because of the dynamics that have been created and the inequity of the situation. Why then do I believe that there is some merit in a posttermination waiting period?

First, most cases of sexual misconduct and abuse take place during the therapy hour. A posttermination period would not apply to these cases. Second, while I am in 100% agreement, in principle, with the "It's never OK" stance, I feel that this absolute position provides no direction out of a hot situation that may be perceived (by both involved) as true love.

Therapy is not a place that should provide dating opportunities for single therapists, yet I have heard too often in presentations by some professionals in the community the advice that if you fall in love, simply terminate, refer the patient, and then see the individual.

Would a therapist voluntarily wait to begin what may be viewed as just a romantic relationship? Does the victim, who

views the therapist in many cases as the only person who can lead the way out of a painful life situation, understand the dynamics of the patient/therapist relationship at the time of a hasty termination? What would a waiting period provide in these cases?

A posttermination waiting period, with no contact between the patient and the therapist, would set forth guidance for both parties. During the waiting period each party would need to undergo independent therapy to sort out feelings of transference, "love," the power differentiation, dependency, and, for the patient, the reason he or she came into therapy in the first place.

The waiting period would set a standard and provide a cool-off period and an opportunity for the patient to learn about therapy dynamics and about the therapist's potential for power and control during a period of patient vulnerability. It could move the relationship out of secrecy into open discussion. It could provide the opportunity for community involvement and accountability.

"It's never OK" may be, in principle, no more than a terrific bumper sticker slogan. The "never" position fails to provide guidelines and leaves unresolved feelings. It may also lead to temptation and sexual contact with, most often, damaging results to both the victim and the physician. My hope is that a posttermination waiting period could be supportive to both parties and may result in a continued no-contact arrangement.

DIANE D. ARONSON
Arlington, Mass.

SIR: Dr. Appelbaum, Ms. Jorgenson, and the *Journal* are to be congratulated for stimulating the vigorous national debate which has followed the publication of their article.

Studies of the beliefs of professionals as to the ethicality of posttermination sex between a therapist and former patient have found that only 50%–60% rate such behavior as never ethical (1, 2). In one study sex with former patients was rated virtually identically to "inviting clients to a social event" and "telling a client of your sexual attraction to them" (1). In discussions with hundreds of professionals over the past 20 years we have found virtual agreement on only one issue: that terminating in order to have sex is unethical.

In our own work, which involves consultation in several thousand cases of therapist-client sex, the vast majority of complaints of posttermination exploitation come in situations where there has not really been a termination or in which there was a "quickie termination" to justify sex. Cases where therapist and client have *no contact* for, say 1 year, are extremely rare, and we often hear about them indirectly—not as a result of a grievance (3).

The few studies cited concerning the long-term persistence of transference (4), focus on long-term dynamic therapy or psychoanalysis. None have examined whether the therapist still has power over the client and whether a sexual relationship would be exploitive. Furthermore, we lack any research on the posttermination situation with briefer therapies, consultations, etc. If one is concerned about undue influence or exploitation, it would seem that developing a friendship or financial relationship would be just as worrisome, although only 14.7% of therapists rated this as "never ethical" (2). As Dr. Appelbaum and Ms. Jorgenson noted, one study even found 29.6% of therapists rating marriage with a former patient acceptable after proper termination of long-term therapy.

Regarding marriage to former patients, do we denigrate or declare such relationships as *a priori* exploitive? If so, what

about the children who result, some of whom also enter our field as therapists? We obviously need more clearly articulated standards, and the solution proposed by some, "It's never OK," doesn't help any more than the current, "It's nearly never OK." Any such standard needs to include 1) a clear definition of termination; 2) a posttermination time interval, which, as Dr. Appelbaum and Ms. Jorgenson noted, must exclude any contact; and 3) that additional criteria beyond the waiting period be defined. Our own work (3) analyzes these issues in greater detail and recommends: 1) a prohibition against sex with former clients of long-term, transference-laden therapies; 2) a 2-year waiting period; and 3) a prohibition against sex with former clients who have special vulnerability due to past victimization.

Once standards are established, we must deal with informed consent. What must clients be told about all of this upon entering therapy? Finally, since the vast majority of cases which led to complaints, or where harm appears to have occurred, involved liaisons within 6 months of termination, our focus needs to be on the major problem: the phony termination or the quickie termination.

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GARY SCHOENER
Minneapolis, Minn.

SIR: Dr. Appelbaum and Ms. Jorgenson have provided a comprehensive and thoughtful review of the legal basis for sanctions of posttermination sexual activity between psychotherapist and patient. They are correct that an absolute lifelong ban on sexual activity would probably not withstand legal challenge and that a 1-year prohibition after termination is a reasonable, justifiable, and enforceable limit. It is important to make the issue more clear, as disciplinary bodies have not had clear guidelines to follow.

Lifetime prohibition of sexual activity is problematic ethically as well as legally. Respect for autonomy is a primary ethical mandate, and it is hard to defend the proposition that a patient can never make an autonomous choice to enter into a sexual relationship with a former therapist. The question of patient autonomy is a difficult one in psychiatry, but certainly we do not want to insist that the act of becoming a patient removes a patient's autonomy for life, even in a limited arena. After all, if returning the patient to autonomy is not the goal of psychotherapy, what is?

We applaud the efforts of Dr. Appelbaum and Ms. Jorgenson to settle on a proposal for an ethical and legal standard that makes clinical sense.

KAREN RITCHIE, M.D.
RAY HAYS, PH.D., J.D.
Houston, Tex.

SIR: Dr. Appelbaum and Ms. Jorgenson have done a great service by frankly addressing the much gossiped about, but woefully neglected, topic of doctor-patient posttermination sexual involvement. I was, however, disturbed by their failure to discuss sufficiently two main points.

First, while there was substantial exploration of the various issues involved and a pragmatic solution of a 1-year grace period after termination was offered, there was, in my opinion, a lack of appropriate outrage at the basic situation. Why are doctors not being urged to examine seriously their motives, countertransference and otherwise, through personal reflection or resumption of their own treatment for such involvement with their (former) patients? While doctor-patient romantic and sexual liaisons have happened historically and are perhaps occurring now in larger numbers, this should not mitigate our concern and calls for serious self-examination each and every time such a transgression happens.

Second, the authors barely discussed the gender breakdown of such doctor-patient pairings and only commented that they nearly always tend to be male doctor-female patient. It is important to know whether female psychiatrists enter into sexual relationships with their patients—in what numbers and under what circumstances. It would be very interesting to compare such data with those gleaned from male colleagues and to explore similarities and differences.

MICHELLE E. FRIEDMAN, M.D.
New York, N.Y.

SIR: As a former Chairman of the Committee on Ethics of the American Psychoanalytic Association and former Editor of the journal *Psychiatry*, I was shocked and dismayed by the recent article of Dr. Appelbaum and Ms. Jorgenson. It is wrongheaded, reckless, and mischievously harmful.

In their discussion of why posttermination therapist-patient sexual contact is "undesirable," the authors omitted almost entirely the damage to the treatment process from violation of the principle of abstinence. They failed to recognize that the purpose of abstinence in treatment is to enable the patient to remember and come to terms with the past pain of refused and lost love and to resist the temptation to give way to a short-cut, magic elixir "love cure."

The promise of future gratification inherent in the idea of a socially sanctioned "waiting period" makes a mockery of the principle of abstinence, of professional ethics, and of the integrity of the treatment relationship, to say nothing of evoking associations to setting waiting periods for handgun purchase or for going through the revolving door from government service to influence peddling.

The authors attempted to support their proposal with casuistic reasoning and slanted, selective use of available data. They asserted that "treatment and the obligations it places on the therapist are time limited" and that "for most purposes the fiduciary relationship ends when therapy is concluded." On the question of how long and in what forms transference persists, they argued that for most patients it diminishes with time, but in actuality the psychoanalytic studies by Pfeffer and by Norman et al., which they cited in support of their argument, give strong evidence of how powerful and easily revived transference effects are and how important enduring elements of identification with the therapist's mode of addressing and solving problems are to the patient's future functioning. The authors selectively omitted these observations. Although they acknowledged weakly that "some data suggest that some patients may retain feelings about their therapists for considerable . . . time," they immediately added the further weakening qualifier, "It is unclear whether

these feelings are of the type or magnitude which would interfere with competent decision making."

We can anticipate rapid consequences from the proposal: it will be popular with many, a number of treatment terminations will be hastened, it soon will be suggested that a 6-month wait may suffice, and defendants and their attorneys in ethics and malpractice cases will eagerly seize upon this article for their defense.

These are but a few of my objections. In addition, the acceptance and positioning of this as the lead article raise serious questions about referee and, I regret to say, editorial judgment. At most, it may belong on an op-ed page, but not in a scientific journal, despite its cloak of scientific form. Its coincidental publication at the same time as PBS's "Frontline" airing of "My Doctor, My Lover" is further cause for dismay.

DONALD L. BURNHAM, M.D.
Bethesda, Md.

SIR: I read with considerable interest and eventual consternation the most provocative article by Dr. Appelbaum and Ms. Jorgenson on psychotherapist-patient sexual contact after termination of treatment. I believe that their proposal has the potential of setting a most dangerous precedent that could result in highly manipulative and nonprofessional behavior in those psychotherapists so predisposed. Indeed, I could foresee the entire therapeutic relationship in some instances totally manipulated by the unscrupulous therapist to fulfill his or her own personal needs.

In making their recommendations, Dr. Appelbaum and Ms. Jorgenson are assuming that our work with patients in psychotherapy is of a finite nature, in that there is a clearly demarcated endpoint. However, given the chronicity of the majority of the disorders that we treat (e.g., severe anxiety-based disorders, major depression, personality disorders, schizophrenia), the high recidivism rates, and as I have pointed out elsewhere (1), the importance of providing booster treatment over extended periods of time after discharge, it is not uncommon for patients to return for retreatment or less intense booster treatment even several years after termination. That being the case, even given the 1-year hiatus in contact between the therapist and patient, I am not convinced that the patient will be able to make an informed and unbiased judgment about entering into a personal relationship with a prior therapist. Indeed, even 1 year or more after termination, the patient's status in relation to the therapist will be of a subservient nature. I agree with Herman et al. (2) and Gabbard and Pope (3) that sexual intimacy between the therapist and patient is tantamount to a breach of the incest taboo. I can see no circumstances under which this taboo can be rescinded. As to Dr. Appelbaum and Ms. Jorgenson's proposal, I say, caveat emptor!

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MICHEL HERSEN, PH.D.
Pittsburgh, Pa.

SIR: It is timely that Dr. Appelbaum and Ms. Jorgenson addressed the issue of posttermination sex during the current national debate on what behavior constitutes sexual exploitation. This is an important but neglected issue and the authors should be praised for addressing it directly. Nevertheless, I believe they reached the wrong conclusions and wish to make the following points.

The authors argued forcefully and correctly that sex during therapy is likely to be harmful to the patient, but went on to state that the reasons for preventing sexual contact are "weaker" for sexual relationships after termination. Although the reasons may be "weaker," that does not mean they are insufficient. Consider the case of a person who maintains some transference feelings after termination that lead to impaired decision making. That person might wish to become involved with an idealized authority figure to defend against inner distress. Our purpose in working with patients is to help them to become more satisfied with themselves and more empowered in their lives, not to help them attach themselves to an idealized authority figure. Since the authors acknowledge the lack of useful data about posttermination sex, shouldn't we be cautious and try to prevent potentially unhealthy behavior by patients?

The authors' argument that posttermination sex could legitimately occur 1 year after termination assumes that therapists are well-meaning, but there are therapists who are malevolent and whose own gratification is their primary concern. What a boon to a predator (and our profession has them) to have a rule explicitly allowing sex with any patient whom one hasn't seen for a year!

The authors' concern that rules forbidding posttermination sex are unconstitutional is primarily a legal one. We should not use legal reasoning to make decisions about what is good patient care when that reasoning requires a thorough understanding of issues outside our area of expertise. Even Supreme Court Justices disagree on what behavior is constitutionally protected. We and our patients are better served if we articulate our patients' complex needs and vulnerabilities, such as posttermination feelings and wishes, and help the legal profession to use their conceptions to serve those needs.

The authors' main argument against a total ban on posttermination sex is that it would preclude "relationships that may involve no more problems than many relationships routinely sanctioned in our society." That society has sanctioned relationships in which power is easily abused is not justification for our sanctioning a relationship that could easily include exploitation as a component. Given our rather dismal behavior in the past in advocating for chronically ill and sexually abused patients, it is perhaps too much to hope that we could take the lead to oppose exploitation, but it would certainly be a step in the right direction for psychiatric organizations not to condone it.

There is a significant potential for harm to a patient in a sexual relationship with a former psychiatrist, and this goes against our primary ethical responsibility as physicians to "first do no harm."

EDWARD H. DRUMMOND, M.D.
Portsmouth, N.H.

SIR: The assumption of Dr. Appelbaum and Ms. Jorgenson, that residual transference from prior treatment interferes with ex-patients' competent decision making concerning sexual behavior with previous therapists, stands in interesting contrast to another article, published contemporaneously by an equally erudite scholar, Professor Slovenko (1). In his article Slovenko stated, "In truth, transference jargon has beclouded common sense."

Transference as a basis for implying aberrant ethics, disgraceful behavior, or even, in some states, crime when it involves posttermination therapist-patient sex represents an absurdity worthy of analysis. Let's face it: all people retain positive or negative residual transferences toward important persons represented during their formative years, most commonly their parents. One would hardly cite residual child-parent transference as decision impairing and as a coercive influence in the case of an adult of average intelligence failing to exercise judgment independent of parental wishes. The capacity for decision making in nonpsychotic and intellectually normal people totally outweighs the assumed mythical power of transference.

What about transferences that develop during the course of group therapy? If society is going to hold psychotherapists liable for posttreatment sexual involvement with former patients, then the next pseudological step would be to hold therapists responsible for transferences that develop between group members in therapy and that escalate into undesirable sexual involvement when the therapy is terminated. Such an argument would conceivably hold a therapist liable for previously exposing ex-patients to transferences with other patients as a result of which, subsequently, the capacity to refuse sex with the transferee is psychologically impaired.

To state that sex with former patients is by and large professionally undesirable is an issue quite separate from blaming impaired decision-making capacity because of residual transference. Such a hypothesis reinforces an unfortunate trend in our society, namely, overemphasis upon vulnerability of, and compensation for, potential victims and underemphasis upon the moral value of doing right instead of wrong.

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THEODORE PEARLMAN, M.D.
Houston, Tex.

SIR: In their article, Dr. Appelbaum and Ms. Jorgenson argued that a sexual relationship between a psychotherapist and former patient is permissible after a 1-year waiting period. I suggest that if the therapist and patient are to engage in intensive psychodynamic psychotherapy, a better rule from the start is that there should never be such a relationship. This prohibition is inflexible, but not needlessly so, and is based on a fundamental view of the nature of intensive psychodynamic therapy and its effect on both members of the dyad.

It is a well-known view that unconscious wishes are timeless and that such fantasies exist unchanged over the years after they first occur. Thus, the wishes which are a part of the child's oedipal constellation are always there, available to emerge in different conscious, derivative forms. Wishes that an adult develops and that are considered dangerous are subject to repression and remain unconscious, but unmodified. Romantic and sexual feelings a therapist feels for a patient could be repressed in this context if the therapist considered them potentially dangerous.

There is also a growing literature that suggests that transferences are an ubiquitous part of everyone's life experience, are probably a way of providing a framework for cognition and perception, are rooted in each person's biopsychosocial endowment and history, and are an important part of many therapists' experiences with many patients with whom there is a deeply probing dynamic relationship (1). To know the patient, the therapist will experience transferences toward the

patient and thus experience intense feelings based not only on his or her consciously known past and present but also on the basis of his or her unconscious past actual and fantasized experiences. Further, some therapists unconsciously identify with their patients (2) or the individuals their patients describe in the therapeutic transference (3). This seems to be a special form of transference, involves the therapist's subconscious past experiences as models, and is experienced by those therapists who allow themselves to be carried more fully into their patients' intrapsychic worlds. This is an essential way for these therapists to learn about their patients, because parallel processes of self-discovery can then occur (2).

Thus, in the crucible of the intensive psychodynamic therapeutic relationship, very strong feelings will be stirred in the therapist as well as the patient. Given the old views I describe about the timelessness of unconscious wishes and the newer ones about the therapist's transferences, identifications, and ways of knowing, it seems prudent for the therapist to afford himself or herself and the patient the insurance of a fail-safe caveat: romantic and sexual fantasies are necessary and proper in the minds of both parties, if such fantasies are a way of understanding the patient's conflicts, but are never permissible in action. Only then can the therapist avoid repression of his or her feelings about the patient, which might prevent understanding the patient during the therapy and/or permit actualization of a previously unconscious wish of the therapist's after termination. Only then will both therapist and patient enjoy the freedom to explore the patient's psychological world in the greatest possible depth.

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STEPHEN M. SONNENBERG, M.D.
Washington, D.C.

SIR: The thoughts that follow are in disagreement with the recent article by Dr. Appelbaum and Ms. Jorgenson. Since I can write only as a psychiatrist, I am addressing only clinical and associated ethical aspects of the article and not its possible legal usefulness.

I think the authors significantly downplayed the endurance of transference and the intensity of its grip even after many years after termination. What the authors seem to be mistaking for a withering away of the transference is more a diminution of the place of transference derivatives in the consciousness of the (former) patient. We really have little reason to believe that the potential for exploitation diminishes nearly so rapidly or even so much over time as the authors seem to think. Further, the potential for the transference to impair decision making by the former patient, and for the lingering countertransference to impair decision making by the former doctor, is similarly long-lived, most especially for matters of great personal emotional import in their relationship to each other. I think the authors' viewpoint is a kind of new edition of an older view, once current in psychoanalytic circles, that adequate interpretation of the transference in the course of treatment actually succeeds in abolishing it. We have, over the decades, learned the hard way that this is not so. The authors now seem to suggest that even if transference is not abolished (or hugely lessened) in the course of treatment, then the pas-

sage of a year without contact with the doctor will finish the job, so to speak. I think this is most naive.

I could foresee a nightmare for any District Branch ethics committee in the event of a filed complaint, trying to decide 1) if a year had in fact passed since the end of treatment, 2) if no significant social contact had occurred during the year, i.e., deciding whether whatever contact occurred, if any, crossed the line, and 3) whether or not, in a given case, one of the various exceptions admitted to by the authors should mandate a permanent proscription of posttermination sexual contact.

There would remain, if we followed Dr. Appelbaum and Ms. Jorgenson's recommendation, the difficult problem of the consenting posttermination patient who, after a (posttermination) affair or even marriage with the former psychiatrist, came to understand that actually residual transference issues had led to the consent. Now we know that transference is an important element in all relationships, including love relationships. In the event of a posttermination marriage or affair turned sour, it would be a particularly daunting task for any ethics committee to attempt to sort out which transference issues derived from the period of treatment and which (if any) did not.

While I agree with the authors about the problems they cited as resulting from our current "almost always is unethical" characterization of posttermination sex, I cannot agree with their solution and would prefer a flat-footed statement that posttermination sexual contact "is unethical."

Of course there would be some abridgment of freedom resulting from a permanent ban on posttermination sexual contact and conceivably a (rare) suitable and nonexploitative relationship would be frustrated. But there is every reason to believe that the cost it would impose would be very greatly outweighed by the grief and mischief such a ban might help prevent.

PAUL E. SAPIR, M.D.
Providence, R.I.

SIR: I read with interest the article by Dr. Appelbaum and Ms. Jorgenson. I differ, however, with their proposal that sexual contact between a therapist and ex-patient be permissible 1 year after therapy has terminated provided certain conditions are met. On the basis of my own clinical experience, I believe that a therapist should never have sex with an ex-patient. Let me illustrate with a brief case history.

Ms. A was a young woman who began twice weekly therapy with a male therapist because of depression and inability to function as an expert in her field. After several years, she overcame her depression and returned to full functioning in her field. Therapy was then terminated to the patient's and therapist's satisfaction.

After termination she saw her therapist at large social gatherings involving mutual acquaintances once each year. At one of these gatherings, 15 years after termination, she had sexual relations with the ex-therapist. This sexual experience was a disaster for the patient. She felt that the therapy had been a fraud. The patient was able to function only in a narrowly circumscribed area as an expert in her field. Otherwise she was miserable and depressed.

After numerous attempts at treatment, she started therapy with me. The rage and suffering expressed by the patient were so intense that she was convinced that she was nearly psychotic, although objectively she was not. Fortunately, in this psychoanalytically oriented psychotherapy,

three times weekly over many years, severe anxiety and conflicts reactivated by the sexual liaison with her ex-therapist were worked through sufficiently for a successful termination. What finally emerged in treatment was the lifting of repression of her sexual experiences with a beloved relative when the patient was 4 years old.

The patient herself was able to see that what had occurred during the first therapy was a transient transference "cure." She understood that she was driven to repeat her past with her kindly relative, personified by her first therapist in the transference. This drive to repeat the past was not consciously known to either the patient or the ex-therapist at the time of the sexual contact.

Transference "cures" like this case are probably commonplace. The therapists and patients are often totally uninformed about repressed psychological issues of both a sexual and an aggressive nature. Even in psychoanalysis, the transference can never be completely resolved. Therefore, it would appear prudent not to take a chance with an ex-patient's psychological health for the ex-therapist's sexual gratification.

In my opinion, there is always a risk of seriously traumatizing an ex-patient if there is posttermination sexual contact with an ex-therapist, no matter how long after therapy has ended. For that reason alone, a therapist should never have sex with his ex-patient.

ALVIN CURTIS SPINDLER, M.D.
Ann Arbor, Mich.

SIR: Dr. Appelbaum and Ms. Jorgenson have written a useful analysis of a major professional problem, the sexualization of the therapeutic relationship after treatment termination. They differentiated criminal law, civil law, common law, administrative boards, and professional societies as they related to this issue. They then implied that their proposal of a "1-year waiting period after termination" would fit the regulatory needs of all agencies.

It would have been more helpful, I believe, if they had stayed with their differentiation. Regulatory agencies, legislatures, and APA have quite different functions, and the "appropriate" position of each will probably not be identical.

While psychiatrists, through APA, are influential consultants to legislatures and regulatory bodies, we alone are fully accountable for controlling our own internal standards of professional ethics. These standards not only help us avoid abusing current and "former" patients but they also help us take care of future patients by creating an ambience that fosters professional pride and public trust and confidence. The therapist's office must be uncommonly safe.

In answering patients' questions about the fee and time structure, confidentiality, and other frame issues in our work, would we feel comfortable with "after termination of the treatment, it is professionally ethical for us to have an intimate social relationship if we both wait 1 year"?

In these times when we are working to improve the public image of psychiatry, who would be harmed by our professional society taking an ethical position that, for purposes of our own, stated, "Once a patient, always a patient"?

THEODORE I. ANDERSON, M.D.
Lexington, Mass.

SIR: Neither Hamlet nor a worried patient will find comfort in Dr. Appelbaum and Ms. Jorgenson's "proposal" that therapists slow their "wicked speed, to post with such dexterity to

incestuous sheets!" by waiting 12 months before having sex with their former patients. Neither the passage of time nor the imprimatur of the wisest consultant can undo the incestuousness of such liaisons.

The authors miss the point. If the "too, too, solid flesh" is actually weak and likely to melt, then the architecture of the therapeutic contract must be strong. Patients and therapists need to know, from the moment treatment makes them vulnerable to their transferences and countertransferences, that the nature of the professional relationship will always remain inviolate. Treatment requires the safety of such a frame. Its anticipated future violability would destroy the therapeutic frame retroactively throughout the course of a treatment.

After all, what forbearance is demanded of psychiatrists? Out of several billion potential partners available for intimate relationships, a hundred or so shall be irrevocably excluded from consideration, in exchange for a good livelihood, an honorable profession, and the (different) gratification of a professionally bound relationship. Is this really a sacrifice before which the profession must quake and tremble?

The article will justifiably frighten many patients, especially those with memories of traumatic violation in their past who already fear for their safety in psychiatric treatment. They will be troubled by psychiatrists' reluctance to be bound by the rules that define the framework of their efficacy. Publishing this article without disclaimer in the *Journal* was a serious error in editorial judgment. "It is not nor it cannot come to good."

PAUL HAMBURG, M.D.
Boston, Mass.

SIR: The scholarly article by Dr. Appelbaum and Ms. Jorgenson sharpens the focus on the pressing ethical problem of psychotherapist-patient sexual contact. At the same time it fails to take account of two basic issues. One of these is the incontrovertible fact that no two persons absolutely *must* achieve sexual connection. Strong desire, even a sense of compulsion, may exist, but the consummation is not a human necessity. That being said, the issue of fiduciary responsibility requires reexamination. The psychotherapist-patient relationship, if not unique, is at least on an order of magnitude more intense than the more general doctor-patient one. The mindset of the patient that endows her or his therapist with special qualities may soften with time, but it does not go away. Posttherapy contact inevitably capitalizes on that fact, whether in a week, a year, or a decade. In that sense, it is inevitably exploitative, varying only in degree. Sexual gratification of the therapist is achieved through exploitation—period! My second point is that the authors' proposal of a 1-year mandatory "waiting period" contains within it a truth that they have not acknowledged. That is the fact that the protagonists are waiting. They are waiting to fulfill a possibly unspoken contract entered into, whether in or out of their awareness, during the course of therapy. The observation that only 1% of cases of posttherapy sexual contact coming to adjudication began after 1 year is beside the point. The potential for harm to the patient is the point. But the therapist is also harmed, by blunting his or her ethical sensibility.

It should be cause for embarrassment that the Florida Board of Psychologists has adopted a higher standard of conduct than we psychiatrists have: the acknowledgment that the psychologist-client relationship is deemed to continue "in perpetuity." In summary 1) we do not have to have that sexual relationship and 2) a codified "waiting period" institutionalizes abuse of a continuing fiduciary relationship. I applaud the proposal of a uniform rule applying to "all treatment provided

by psychiatrists and nonmedical psychotherapists." Let it take these issues into account.

GEORGE E. MURPHY, M.D.
St. Louis, Mo.

SIR: Dr. Appelbaum and Ms. Jorgenson presented an interesting and controversial proposal regarding psychotherapist-patient sexual contact after termination of treatment that attempts to be both sensitive to the issues and simple to apply. I have concerns, however, about the narrowness of their focus and the implicit assumption that psychiatrists should be lumped with nonmedical psychotherapists rather than with their medical colleagues. While the authors noted that psychiatrists engage in a variety of relationships with patients, ultimately they made the assumption that all psychiatrists are defined, for their purposes, as psychotherapists. They feel that it is impossible to distinguish when the relationship crosses the line from a more "medical" role into a psychotherapeutic one. While unable to distinguish a line between psychiatrists and psychotherapists, they have, in fact, established an arbitrary boundary between psychiatrists and other physicians.

Clearly, the appropriate boundaries of the complex relationship between individuals and their psychotherapists need to be considered with extreme care. At the same time, however, this is an issue which should also be specifically addressed in other professional settings. On what basis have the authors excluded nonpsychiatric physicians (or for that matter, other professionals, such as lawyers) from their proposal? The factors associated with societal limitations on individual choice, i.e., impaired decision-making capacity, coercion, and fraudulent representation, can all apply to other professional relationships with similar "power imbalances" (for example, gynecologists and their patients, bankers and loan applicants). While transference issues are obviously most pertinent to the psychotherapeutic relationship, it is a phenomenon implicit in all human relationships. I would be interested in where and how the authors would apply these or similar guidelines to other professional groups.

HAROLD ALAN PINCUS, M.D.
Chevy Chase, Md.

SIR: I read with interest Dr. Appelbaum and Ms. Jorgenson's recent article. I am not sure what the best time interval should be before posttermination patient-therapist sex might be legally permitted, although I think the effect of transference is frequently much longer than the authors imply.

An important side effect of the increasing societal penalties for therapist violation of the sexual taboo with patients is that what used to be a matter of integrity or pride for the appropriately abstinent therapist is now becoming only a matter of coercion for the scoundrel. We have all lost something when our behavior as therapists is increasingly regulated.

JOEL KOTIN, M.D.
Laguna Beach, Calif.

SIR: It is an unfortunate reflection of the preoccupation of our society with genital activities that Dr. Appelbaum and Ms. Jorgenson, in their otherwise superbly thoughtful review, should fail to consider the most common setting for sexual contact in our society: marriage.

The authors noted that the specific elements providing the basis for restricting therapist-patient sexual contact—the pa-

tient's impaired decision-making capacity, the power differential favoring the therapist, and the likely dishonesty, covert or overt, in the situation—while perhaps no less commonly found in ordinary sexual encounters, provide a valid basis for such restrictions in therapist-patient encounters because of "the unfairness of allowing the psychotherapist to benefit from the patient's compromised decision process while the patient risks substantial harm." Although it might be argued that while nonmarital sexual contact between therapist and patient, as a purely private behavior, insofar as it does not afford a remedy to an injured or exploited party, warrants anticipatory supervision to prevent injury or exploitation where the risk is predominately one-sided, marriage, where both parties are at risk, does not require such supervision, since divorce laws provide a remedy for the injured party should the relationship fail.

I suggest that this is a specious argument. Abusive, exploitative marriages in our society are hardly uncommon. They are often held together by the very pathological interactions that brought them together (until they fall apart when one of the parties has been so damaged by that interaction as to be unable to continue). This is rather late for providing a remedy, especially when the parties were originally brought together in the societally structured therapist-patient encounter, and as Fitzgerald painfully portrayed in *Tender Is the Night*, when the parties are psychiatrist and patient, the victim is not necessarily the patient.

The proposal advanced by Dr. Appelbaum and Ms. Jorgenson is well reasoned and based on data, however limited, rather than on abstract theoretical formulations. I suggest that it be clearly extended to include posttermination therapist-patient marriage, even in the absence of premarital sexual contact.

SIMON L. AUSTER, M.D., J.D.
Bethesda, Md.

SIR: I found the recently published proposal by Dr. Appelbaum and Ms. Jorgenson on psychotherapist-patient sexual contact after termination of treatment to be of interest, but to be unsupported by the analysis which the authors provided. I would question the rationale which they put forward to support their proposal.

The argument for the 1-year waiting period is to allow transference issues to diminish, to avoid coercive influences, and to allow adequate time for the therapist to reflect on the desirability of the proposed involvement. The authors went on to note that if this 1-year period of abstinence is observed, a sexual relationship is seldom initiated. Their own experience described only one case out of more than 100 where such contact between a therapist and a former patient began more than 1 year after the termination of treatment. They then cited the Minneapolis experience where again fewer than 1% of cases of therapist-patient sexual contact began more than 1 year after termination. This seems to me very strong evidence that "appropriate" therapist-patient sexual contact after termination of therapy occurs only rarely.

It would seem that the authors are going to great lengths to justify a behavior that occurs less than 1% of the time. Ninety-nine percent of the time sexual contact occurs less than 1 year from the termination of therapy and is inappropriate by the authors' standards. And even in the 1% that does occur after the 1-year period, there is no assurance that all of the issues of concern that have been raised regarding lingering transference issues, coercive elements, etc. are resolved. In addition we have the very real concerns that Gabbard has so clearly spoken to regarding the contamination of therapy by the

knowledge that such a relationship could be possible in the future. It seems unjustified to contaminate so many ongoing therapeutic relationships with this possibility, particularly when an outright prohibition will be the appropriate position in more than 99% of the cases.

With such a relationship being so rarely appropriate, I prefer to see our profession strongly support the rule rather than the rare exception. In my opinion the APA's position that "sexual involvement with one's former patient is . . . almost always unethical" remains the appropriate stance.

STEWART SHEVITZ, M.D.
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SIR: I write to express concern over the apparent erosion of the editorial independence of the *Journal*. As reported in *Psychiatric News* (1), a recent article by Dr. Appelbaum and Ms. Jorgenson (2) caused considerable controversy within the profession. Also according to *Psychiatric News* (1), the Editor of the *Journal* acquiesced to pressure from the APA Board of Trustees to allow a belated editorial response to the article from the Chair of the APA Ethics Committee.

Although I fully support open debate and discussion of controversial issues and opinions published in the *Journal*, I am concerned that undue influence from the Board or other groups within APA will actually diminish the editorial independence and scientific integrity of the publication.

The article by Dr. Appelbaum and Ms. Jorgenson was reviewed and accepted through the established blind peer review process. Decisions regarding subsequent discussion and debate of this or any other article published in the *Journal* should be left entirely to the discretion of the Editor and editorial review board.

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Dr. Appelbaum and Ms. Jorgenson Reply

SIR: We are pleased to have stimulated such a lively debate on an important, but infrequently addressed issue. Our particular thanks go to John Nemiah, M.D., for his consistent willingness to open the pages of the *Journal*—in this, as in other instances—to the discussion of contemporary problems of major significance for psychiatry.

Given the diverse opinions expressed by us and our many correspondents, it may be useful to underscore one conclusion about which we all agree. Everyone concurs that sexual relationships between psychiatrists and their current patients are so likely to be exploitive and harmful that they should always be considered unethical. Indeed, given the difficulties the profession has had deterring such behavior, we favor making psychotherapists' sexual contact with patients a criminal offense.

There is less consensus, however, on parameters for post-termination relationships. The APA's rule since 1988 has been that sex with a former patient is "almost always unethical"

(1). (Prior to that APA had no formal position, and it was an open secret that many psychiatrists and other therapists had married former patients.) This position offers little guidance to therapists and provides little protection to patients, since the temptation exists to see every relationship as the exception envisioned by the rule. As Ms. Aronson says, "I have heard too often in presentations by some professionals in the community the advise that if you fall in love, simply terminate, refer the patient, and then see the individual." But hasty termination and immediate sexual contact with former patients may be as damaging to former patients as sexual contact during therapy. The current APA rule is clearly inadequate.

In our effort to devise an alternative approach more protective of both patients and therapists, we analyzed the factors that contribute to the exploitive nature of patient-therapist sexual relationships: patients' substantially impaired decision making, and the possibilities of coercion and fraud by therapists. We argued that as time passes after termination, with no further contact between patients and therapists, the salience of these factors diminishes, until a point is reached at which sexual relationships can no longer be considered exploitive. Recognizing the difficulty of line drawing, we proposed that sexual relationships with former patients that begin within 1 year after the last contact between therapist and patient be considered unethical per se. Should such relationships begin after 1 year with no contact whatsoever between patient and therapist, however, we argued that the risk of exploitation is sufficiently diminished and that there is insufficient justification for prohibition.

By proposing this rule it was *not* our intention to encourage sexual relationships with former patients. Indeed, compared with the indeterminate state of the current APA ethical guidelines on posttermination sexual relationships, we hope that our proposal will have the opposite effect. Since almost all intimate relationships now begin within 1 year after termination, our proposal should have the effect of diminishing the frequency of such relationships.

Our correspondents offer four main objections to our analysis, which we will consider in turn. Several writers urge that—by holding open the possibility of an intimate relationship in the future—our proposal would corrupt the course of therapy, which will deteriorate into verbal courtship or foreplay. Of course, the same could be said of the current APA position, which leaves open the possibility that any therapeutic relationship, with no interval whatsoever, could evolve into an intimate one. The current rule, whatever its deficiencies, has hardly led to the breakdown of boundaries in psychotherapy and the corruption of the therapist-patient relationship. Nor would our proposal.

In fact, compared with the status quo, a 1-year waiting period would be more protective of patients' interests. The "predatory" therapists whom Dr. Drummond fears we would encourage are not—we can state with assurance, having seen them in action in many cases—the kind of persons who will discontinue treatment, then wait 1 year without any further contact to initiate sexual relationships. As for the "love-sick" therapists about whom Dr. Gabbard has written (2), they will have a long interval in which to work through their countertransferences and obtain help for their own problems. Patients, too, freed of regular contact with an imposing authority figure, will have an opportunity to sort through their feelings and seek assistance in resolving them. Under our proposal, the consulting room would become a safer, not a more treacherous place.

A second objection is that—even if therapy is not impacted directly—we underestimate the persistence of former patients' transference to their therapists and the consequent enduring

impairment in their abilities to make decisions about relationships. It would be unfair, according to this argument, to allow former patients to enter into intimate relationships, even after a substantial period has passed. Perhaps that is true, but despite several letters' claims to the contrary, the empirical literature on transference lends little support to this assertion. The major studies, which deal solely with patients who have been in analysis, have serious methodological problems (3–5). Indeed, given the small number of subjects involved, they are more in the nature of case reports than systematic research. Further, the results of these and other studies (6, 7) are sufficiently ambiguous that they can be interpreted equally well as indicating the rapid diminution of transference over time as the contrary. Moreover, the research on transference has never addressed the most relevant issue for our purposes here: granting that patients will continue to have some sort of feelings about their former therapists, are those feelings generally of the nature and intensity to impair their decision making?

The absence of reliable research in this area is understandable. Transference, as several of the letters demonstrate, is an elusive concept, subject to definitional controversies and ill-suited to precise assessment. How should rule making deal with this problem? The current APA approach is to charge ethics committees with the responsibility for investigating the degree to which a relationship results from a former patient's "projection of feelings appropriate to another person at another point in time" (8). How many relationships could stand such a test? This is a recipe for idiosyncratic decision making of dubious validity.

We would take another approach. As Dr. Sonnenberg notes, correctly in our view, "Transferences are a ubiquitous part of everyone's life experience," including as Dr. Sapir points out, their love relationships. Rather than encouraging inquiry into whether a particular transference so impaired decision making as to warrant invalidating a person's choice—an approach that gives no prospective guidance—we would place the emphasis elsewhere. Common sense and clinical experience suggest to us that the intensity of transference diminishes over time without contact. A flat ban on intimate relationships during a period when transference effects are likely to be maximal seems a more reasonable and fairly administered approach. Several experienced practitioners who have written to us directly have suggested that a 2-year waiting period would be preferable to the 1 year we suggest. It may be. The precise interval is less important here than the idea of a fixed period.

A third contention offered by several writers is that our proposal ignores the likely consequences of posttermination relationships. Dr. Brown and colleagues cite limited data from a highly selected sample of persons who engaged in posttermination relationships, then sought subsequent therapy, to support the contention that most former patients will be harmed (9). In so doing, they ignore the authors' warning that "threats to the validity [of the data] are numerous." Even if these data are accepted as an accurate portrayal of the status quo, however, they have little relevance to our proposal. Most posttermination relationships now begin shortly after therapy ends, often having been arranged while treatment was in progress. That would not be possible under our approach. Thus, the data cited by Dr. Brown et al. tell us nothing about the likely consequences of our proposal.

In contrast, Dr. Schoener at the Minneapolis Walk-In Counseling Center (personal communication), whose clinic probably has the greatest experience with persons who engaged in intimate relationships with current and former therapists, reports a different impression. The vast majority of cases of which he is aware that began a year or more after termina-

tion started with unplanned social encounters between therapists and former patients. Moreover, almost all of these came to his attention through routes other than complaints by the former patients and involved no allegations of harm. To our mind, although both Dr. Schoener and Dr. Spindler affirm that harm may sometimes result, the question of its frequency is an open issue.

The final challenge to our proposal is in many ways the most important, and builds on the previous objections. If lingering effects of transference *may* affect former patients' decision making, even years after termination, and if harm *may* sometimes result from posttermination sexual contact, why should we risk these effects, whatever their frequency? Would a permanent ban on posttermination sexual relationships not be the best solution of all?

Regulation of posttermination relationships involves a balancing of several important considerations: a desire to protect former patients from the adverse consequences of their decisions to engage in intimate relationships with their therapists and their rights (and therapists' rights) to privacy and freedom of association. This conflict between paternalism and autonomy (to use the ethical, rather than the legal terms) arises whenever rule making aims at controlling private behavior. Our constitutional system has worked out a compromise: when the state seeks to infringe on citizens' fundamental rights, it must prove a compelling interest to do so, and even then it must choose means that are least restrictive of those rights (10).

With regard to sexual relationships between patients and current therapists, we believe the likelihood of harm and the unfairness to patients establishes a compelling interest in regulation. Moreover, we are persuaded that no less restrictive means than a total proscription will be effective. As described above, however, the case is much less clear when it comes to posttermination relationships. The vast preponderance of harm comes from relationships begun soon after termination. With a substantial waiting period, neither harm nor impairment of patients' capacities to make their own decisions has been demonstrated. In such a context, no compelling state interest supports a permanent ban on posttermination relationships. The state's interests in protecting former patients—a real one—can be achieved less restrictively by the sort of time-limited ban we have suggested.

Drs. Anderson and Drummond, however, ask why a "legal" analysis should dominate here. Can APA not elect to adopt stricter standards than would be sanctioned by the law? The answer is that, as a private organization, APA is not bound by constitutional considerations in the same way as is a state. But there are two reasons why it would be a mistake too readily to reject the constitutional argument outlined above. First, in our view, there is little difference in this case between the issues that enter into a constitutional analysis and those that ought to be considered from an ethical perspective. Autonomous choices about intimate relationships ought to be respected in general, barring strong countervailing reasons for not doing so. Ethics and law differ little in this regard.

More important still is the question of what impact we want our ethical rules to have. If they are to serve as guidelines for licensing boards and courts, who in contrast to APA can impose meaningful sanctions, they must abide by constitutional desiderata. There may be some autarkic satisfaction in creating a rule of presumed ethical purity, but there is much more impact in creating a standard that can be widely adopted in our society, and stands some chance of serving as a useful deterrent.

We note, in this regard, Dr. Pincus's question as to how our analysis would apply to other, nonpsychotherapeutic, and even nonphysician groups. He notes, and we concur, that re-

relationships other than the therapist-patient one, including doctor-patient, lawyer-client, teacher-pupil, and supervisor-supervisee, are plagued with questions about the appropriateness of subsequent sexual contact. A virtue of the approach we suggest is that it serves as a model for other relationships in which similar problems of impaired decision making, coercion, and fraud may arise. The right answer may be to prescribe intimate relationships until some time has passed after the professional relationship has ended.

Given the limitations of space, we apologize for not being able to address every question raised by all of our correspondents, but we look forward to continuing discussions in the pages of the *Journal* and elsewhere.

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Tranylcypromine Abuse: Cause for Concern?

SIR: The recent case report by Kathleen Theresa Brady, M.D., Ph.D., and colleagues (1) highlights the possible abuse potential of tranylcypromine. It is the only monoamine oxidase inhibitor (MAOI) that has been linked to abuse potential, which seems to be related to its amphetamine-like properties. This includes a chemical structural similarity to amphetamine as well as some metabolism to amphetamine (2). Chronic use of tranylcypromine can lead to habituation and a withdrawal state. These withdrawal effects are unpleasant and not too prolonged except in those rare cases where the drug has been abused (3). It is clear that although such cases do indeed occur, they are extremely rare. This is brought out by the fact that in a 1969 book on MAOIs (4), among other psychoactive drugs, there was no evidence that chronic treatment with MAOI induced physical dependence or withdrawal symptoms after termination of treatment. It is clear that the rarity of tranylcypromine abuse is due to the fact that its abuse is directly related to its amphetamine-like properties and to its

partial metabolism to amphetamine; which seems only to occur at very high dosage levels of the agent. Such high doses invariably cause marked CNS stimulation and delirium, as was found in the case reported by Dr. Brady and colleagues, where doses of approximately 300 mg/day were ingested (1). This dose seems to be close to the fatal dose of tranylcypromine, since a successful suicide with this agent at an acute dose of 500 mg has been recorded (4).

In order to prevent even the rare occurrences of tranylcypromine abuse, it seems essential to forewarn the patient of its abuse potential and the potentially fatal outcome of such abuse. Monitoring of patients who respond rapidly and dramatically to therapeutic doses of tranylcypromine would seem essential, since it is this type of patient that appears to run the greatest risk of abuse.

It must be emphasized that this valuable antidepressant should not be eschewed for fear of its abuse potential, which is extremely low and which can be obviated by appropriate counseling and monitoring.

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FREDERICK J. LICHTIGFELD
MARK A. GILLMAN
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Dr. Brady and Associates Reply

SIR: We would like to thank Drs. Lichtigfeld and Gillman for the interesting and thoughtful comments which they offer. They suggest that the lack of physical dependence and withdrawal after chronic treatment with MAOIs helps to explain the rarity of abuse of these substances. It is important to note that production of physical dependence can be independent of the abuse potential of a drug. Some very common drugs of abuse, including marijuana and cocaine, do not produce clear-cut physical dependence. While it is indeed true that the MAOIs do not produce physical dependence, this does not necessarily have much bearing on the abuse potential of this group of agents.

We agree with the assertion that tranylcypromine abuse is rare, but we feel that it is important to note that the cases reported in the literature all involve individuals with a history of substance abuse. This fact coupled with the increasing prevalence of substance abuse could lead to increased MAOI abuse in the future. More importantly this may help to identify a patient group at risk for abusing these substances, so that they could be targeted for more careful counseling and monitoring when MAOI treatment is initiated. We agree completely with the authors' assertion that these are valuable therapeutic agents which can be safely used when properly monitored.

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Charleston, S.C.

Dynamic Cognitive Therapy Anyone?

SIR: Kenneth Z. Altshuler, M.D., in his review of *Cognitive Therapy of Personality Disorders* by Aaron T. Beck and Arthur Freeman (1), noted with a wink the concordance of cognitive and psychodynamic therapies for personality disorders. Dr. Altshuler noted similarities regarding transference, explorations of the past, countertransference, and the need for frequent therapy sessions for extended periods. He said this made him "rather wonder."

I wonder, too, why no one has melded cognitive and dynamic theory in the grand fashion of our best but disparate cognitive and dynamic theorists. Call it "dynamic cognitive therapy." I can think of no better therapist than one capable of dynamic understanding and interpretation, who can use cognitive techniques to help patients put into action the fruits of their psychodynamic insights. This hybrid therapy no doubt occurs in offices around the globe, by accident or design. What is missing is academic sanction by formal attention and fleshing out of the details.

There are suggestions today that in order to prove psychotherapeutic efficacy (and perhaps to justify reimbursement?), we must follow a given "instruction manual" for a given psychotherapy. We might do ourselves a favor to acknowledge more formally that good therapy can borrow from separate camps. Our separate camps may not be so separate.

Back to dynamic cognitive therapy. Is anyone out there developing this? I would be interested in hearing from you.

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Reprints of letters to the Editor are not available.

THE AMERICAN JOURNAL OF PSYCHIATRY

Special Articles

Psychodynamic Psychiatry in the "Decade of the Brain"

Glen O. Gabbard, M.D.

***Objective and Method:** To illustrate the continued relevance of psychodynamic thinking in the practice of contemporary psychiatry, the author reviews a number of studies that demonstrate the intimate connection between psychosocial and neurophysiological factors in the etiology and pathogenesis of psychiatric disorders. A survey of three specific anxiety disorders illustrates the complex interaction between mind and brain in these disorders. **Results:** Research on both primates and humans suggests that psychological influences result in permanent alterations of a neurobiological nature. Similarly, psychological interventions in a treatment context may have a profound impact on neurophysiology. Clinical case examples demonstrate that "biologically based" disorders may be rich in unconscious meaning. Clinical understanding of the meaning of symptoms may be instrumental in ensuring patients' compliance with pharmacotherapy regimens and in the removal of other resistances to treatment. **Conclusions:** In contemporary psychiatry, a psychodynamic perspective must be preserved. Without it, meaning will be lost, and both diagnostic understanding and informed treatment planning will suffer as a result.*

(Am J Psychiatry 1992; 149:991-998)

Now that the "decade of the brain" is well launched and remarkable discoveries from the neurosciences fill the pages of our journals, the time may be ripe for a reexamination of the continued relevance of psychodynamic thinking to both clinician and researcher. Two trends in contemporary psychiatry have been increasingly disconcerting to those of us who view clinical work as an optimal integration of mind and brain: 1) the "either-or" polarization of the psychodynamic and the biological and 2) the devaluation of psychodynamic understanding and therapy as increasingly irrelevant. Psychodynamic psychiatry is not inherently "antibiological," and it has much to contribute to modern clinical practice.

In asserting the continued applicability of dynamic approaches, I wish to clarify that I am conceptualizing

psychodynamic psychiatry as much broader than dynamic psychotherapy, which is but one component of the dynamic psychiatrist's armamentarium. As I have noted elsewhere (1), "Psychodynamic psychiatry is an approach to diagnosis and treatment characterized by a *way of thinking* about both patient and clinician that includes unconscious conflict, deficits and distortions of intrapsychic structures, and internal object relations" (p. 4). This mode of thought includes such factors as unconscious meaning and the reexperiencing of past relationships in the present with the clinician. Within the broad scope of this definition, treatment measures other than psychotherapy, such as dynamic pharmacotherapy and dynamically informed hospital treatment, are aspects of dynamic psychiatry.

PSYCHOLOGICAL VERSUS BIOLOGICAL ETIOLOGY

Much of the polarization between the biological and psychodynamic perspectives arises from a failure to appreciate the complex relationships between psychoso-

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cial and neurophysiological factors in the etiology and pathogenesis of psychiatric disorders. It is commonplace in clinical practice today to hear patients report that they have been told they have a "chemical imbalance." This oversimplified and reductionistic explanation is problematic from a number of standpoints (2-4). Lipowski (2) expressed his concern as follows:

It confuses the distinction between etiology and correlation, and cause and mechanism, a common confusion in our field. It gives the patient a misleading impression that his or her imbalance is *the* cause of his or her illness, that it needs to be fixed by chemical means, that psychotherapy is useless, and that personal efforts and responsibility have no part to play in getting better . . . To assume, as we all do, that biochemical processes underlie mental activity and behavior does not imply that they are the causal agents but rather constitute mediating mechanisms. They are influenced by the information inputs we receive from our body and environment and by the subjective meaning of that information for us. It is that meaning which largely determines what we think, feel and do. (p. 252)

Neurochemical and neuroanatomical changes in the brain may be causally related to psychosocial influences in the environment and to the meaning attributed to those influences. As a corollary to this point of view, psychotherapeutic interventions may result in permanent alterations in brain functioning. In a much touted series of experiments with the marine snail *Aplysia*, Kandel (5-7) convincingly demonstrated that the functional effectiveness of synaptic connections can be altered by learning experiences connected with the environment, specifically, through regulation of gene expression. Kandel (5) concluded, "It is only insofar as our words produce changes in each other's brains that psychotherapeutic intervention produces changes in patients' minds. From this perspective the biological and psychological approaches are joined" (p. 1037). Although psychotherapy uses the language of meanings, there can be little doubt that inasmuch as events of learning and memory have an impact on the brain, it can be viewed as a biological process (6).

The phenomenon of kindling may illuminate some of the processes involved in the triggering of neural mechanisms by psychological/environmental etiological factors. Gold et al. (8, 9), drawing on the work of Post et al. (10), postulated that painful events, such as separations or losses, early in life may sensitize receptor sites, leading to vulnerability to recurrent depression in adulthood. They pointed out that ideas and images associated with depressive states could ultimately act as conditioned stimuli capable of eliciting a major depressive episode even without a concrete loss or external stressor in the environment. This model is in keeping with the observation that chronic stress and loss early in life may leave people vulnerable to depression as adults. The model is also consistent with psychoanalytic observations that an imagined loss or a perceived discrepancy between idealized expectations and reality may precipitate depression. Gold et al. concluded from this model that major depression is best treated with a

combination of medication and psychotherapy, because the inner conflict brought on by prior life events may increase the burden of stress unless it is addressed psychotherapeutically. They also pointed out that simple equations of depression with single neurotransmitters are no longer tenable, as our knowledge of the complexity of the neurotransmitter systems has increased with more and more sophisticated neuroscience research.

Primate research has been of extraordinary heuristic value in demonstrating the impact of psychological trauma on brain functioning. Squirrel monkeys separated from their mothers experience elevated plasma cortisol levels. If the separations are repeated, these physiological changes become permanent (11, 12). Primate research also suggests that the opioid system is intimately involved in the regulation of separation anxiety and that social isolation has a direct impact on the sensitivity and number of brain opiate receptors (13). Other long-lasting neurobiological changes resulting from early maternal separations include changes in adrenal gland catecholamine-synthesizing enzymes (11, 12), changes in hypothalamic serotonin secretion (14-16), and lasting alterations in the sensitivity of noradrenergic receptors (17). Imipramine and other agents that increase noradrenergic activity at the synapses alleviate the effects of separation and social isolation in monkeys (18).

The psychodynamic notion that psychological trauma may be more or less damaging, depending on the critical developmental phase during which it is inflicted, is also supported in principle by primate studies. In Suomi's research on the impact of maternal deprivation (19), the effects of removing infant monkeys from their mothers were much more striking if the separation occurred at 90 days than if it occurred at either 60 or 120 days, possibly because of a link between myelination of the nervous system and certain kinds of bonding behavior (13).

After an extensive review of the primate research, van der Kolk (13) concluded:

There may be actual morphological changes in the brain following social deprivation, or other disruptions of affiliative bonds. There also is evidence that the number and nature of brain receptors for particular neurotransmitters can continue to change throughout a person's lifetime, as illustrated by dopamine receptor alterations leading to the clinical symptoms of tardive dyskinesia . . . Thus it is conceivable that receptor changes induced by early deprivation or trauma in the CNS can to some degree be modified by later life experiences. (pp. 50-51)

These primate studies not only support the kindling model based on psychological trauma, such as separations, but they also lend credence to the idea that the brain is possessed of remarkable structural plasticity. We now know that morphological changes in brain cells occur nearly every day and that massive trauma is not necessary to induce such changes (20-22). The influence of psychosocial factors on neurobiological

processes can be seen in changes that occur as a result of psychotherapy as well as in pathological states, such as posttraumatic stress disorder (PTSD), in which recurring intensive stimulation from the environment exceeds the capacity of the cortex to process what is happening and leads to synaptic changes of a permanent nature. The fact that one person will respond with PTSD to a situation that leaves no permanent mark on another reflects the fact that the subjective meaning given to the environmental stimulus is critical in effecting synaptic changes.

Conversely, one can also observe the impact of biology on psychology in the aging process. As Roose and Pardes (21) have suggested, the well-known "mellowing" phenomenon of middle age, associated with a shift to more mature defenses (23), may well be linked to the dramatic drop-off in the amount of norepinephrine in the locus ceruleus between the ages of 40 and 60.

The foregoing survey of the mutual influence of psychology and biology in the human psyche attests to the inseparability of brain and mind. A number of leading figures in our field (2, 3, 24-28) have warned of the dangers inherent in the "remedicalization" of psychiatry—namely, that psychiatry might become "mindless." Mindless psychiatry loses the domain of meaning. The essential role that meaning plays, even in disorders with significant biological underpinnings, can be illustrated by a detailed examination of three common anxiety disorders.

OBSESSIVE-COMPULSIVE DISORDER

There is abundant evidence that obsessive-compulsive disorder is an illness with a strong biological component. Monozygotic twins have a higher rate of concordance for the disorder than their dizygotic counterparts, there is an increased prevalence of the disorder in patients with Tourette's syndrome and in their families, and there is a dramatic response in some patients to psychosurgery and clomipramine (29-31). A quantitative study in which computerized tomography was used also demonstrated a smaller caudate nucleus volume in patients with obsessive-compulsive disorder than in healthy control subjects (32). Finally, patients with obsessive-compulsive disorder show virtually no response to placebo, in contrast to patients with other anxiety disorders (33).

To provide a convincing case for the ongoing relevance of psychodynamic thinking in contemporary psychiatry, there must be a demonstrable advantage to a psychodynamic approach. However, there is little evidence in the literature to suggest that dynamic psychotherapy or psychoanalysis is effective in the treatment of obsessive-compulsive disorder (34). As the following case illustrates, however, dynamic principles are of great value even in the treatment of "biologically based" disorders, and the somatic therapies used to treat them are often imbued with psychodynamic meanings.

Case vignette. Mr. A was a 29-year-old unmarried man with obsessive-compulsive disorder. At the time he presented for psychiatric hospitalization, he reported a 10-year history of obsessive-compulsive symptoms, and he complained of being totally housebound for the last 8 years because of constant, incapacitating, "grotesque, horrific" thoughts that never ceased. Eight years before admission, when Mr. A became housebound, his mother retired from her job so she could take care of him at home and meet his demands for cleanliness. Her life revolved around him.

Mr. A was obsessed with the need to avoid contamination. He also worried about making women pregnant, because he feared he might have semen on his hands. Hence, he became a compulsive hand washer. He insisted that his mother had to be with him 24 hours a day. Although she did not sleep with him or go into the shower with him, she did help him dress so that he would not touch his clothes and become contaminated. He also required her to follow an elaborate 58-step ritual while cooking his food and placing it on the table. If she did not follow this ritual precisely, she had to discard the entire meal and start over again. She threw out thousands of dollars worth of food each year in order to respond to these demands. Mr. A also insisted that his father either stay away from home or remain in another part of the house so he would not be contaminated by germs that his father brought home from work.

Mr. A's early childhood development was reportedly unremarkable, but he did recall a very unpleasant event when he was approximately 5 years old. He remembered seeing his father grab his mother by the breasts while she cried for the patient to rescue her. He tried to stop his father, but he was overpowered by the older man. He remembered feeling terrible about the incident, and he cried because he was unable to rescue his mother.

Although Mr. A had been to numerous psychiatrists, he always refused to go back after one visit. At one time he agreed to take clomipramine, but he stopped after the first dose because he said the side effects bothered him. His parents finally felt that they had to hospitalize him because he was incapacitated. When he came to the hospital, I asked him why he was seeking treatment. He responded, "I'm determined to be dependent—I mean, independent." I commented to him that he had first said "dependent," and I inquired, "Is there perhaps a part of you that would like to be dependent?" Mr. A responded, "You mean on my mother?" I replied that I thought he would know better than I. Mr. A reflected a moment and said, "Well, she does take pretty good care of me."

Mr. A's slip of the tongue provided a glimpse into the unconscious motivations for his resistance to treatment. Any kind of successful treatment threatened his dependent relationship with his mother. If clomipramine were likely to help him, then he would not take it. Similarly, he would defeat all other outpatient or inpatient treatment efforts as well.

After about a week of hospitalization, Mr. A defied my expectations. He began to make dramatic improvements. He could touch doorknobs without fearing contamination, he could read magazines that others had touched, and he greatly decreased the time he spent washing his hands. This improvement occurred without medication. Mr. A commented that he felt "a lot less nervous" in the hospital than he had expected. As I explored with him how the hospital setting might have reduced his anxiety, it became apparent that he had been increasingly worried about his sexual wishes toward his mother. He commented that when his mother dressed him, he felt that "there was something sexual about that." Removing him from the emotionally charged household made his sexual

wishes toward his mother much less problematic for him. Similarly, aggressive wishes to keep his father out of his life were less troubling. Because his anxiety about both sexual and aggressive wishes had diminished, his obsessive-compulsive symptoms were not needed so extensively to bind his anxiety.

The case of Mr. A beautifully illustrates the interface between the psychodynamic and the biological. However biologically driven his obsessive-compulsive symptoms may have been, they also revealed a symbolic wish to win his mother's affection away from his father, as poignantly depicted in his early childhood memories. His symptoms reflected the core psychodynamic concept known as compromise formation; that is, they contained both the direct expression of an underlying wish and a defense against that wish (35). Mr. A's compulsive rituals served as a defense against his sexual longings for his mother by consuming all his time in hand washing and various other exercises. However, these symptomatic rituals also resulted in his being dressed by his mother and receiving all her attention, while his father stayed away from home. Hence, the symptoms had the dynamic meaning of fulfilling his childhood wish to steal his mother away from his father. Taking clomipramine or receiving any other form of treatment threatened this triumph by putting him in a position in which he no longer needed his mother. On the other hand, this oedipal victory created enormous anxiety and guilt, which increased his recourse to rituals and obsessions. When removed from the triangle he had established with his parents at home, Mr. A had much less need of his obsessive-compulsive symptoms to deal with the anxiety and showed remarkable improvement.

Consider an analogy: when a magnet is placed under a sheet of paper containing iron filings, the filings line up in formation on the surface and follow the movement of the magnet along the underside of the paper. In a similar manner, psychodynamic issues frequently appropriate magnet-like biological forces for their own purposes. In this manner Mr. A's unconscious wishes and his defenses against them attached themselves to the biologically driven obsessive-compulsive symptoms and used them as a vehicle for their expression.

Although formal dynamic psychotherapy was not used in the treatment of Mr. A, the dynamic understanding of his resistance to pharmacotherapy and to treatment in general was essential in explicating his refusal to take clomipramine and to cooperate otherwise with treatment. In fact, Mr. A's slip of the tongue led to his awareness that any improvement in his symptoms might cause him to lose his privileged position with his mother.

The case of Mr. A also underscores the importance of a psychodynamic approach to pharmacotherapy for cases in which compliance is a problem. Failure to comply with pharmacotherapeutic regimens often can be understood along conventional lines of transference, countertransference, and resistance issues (1). A considerable literature on the practice of dynamic pharmacotherapy has accrued (36-45), and there has been a

broad consensus that psychodynamic meanings of medications may pose formidable obstacles to compliance with medication regimens.

PANIC DISORDER

Nearly 100 years ago Freud (46) identified two forms of anxiety. One form, which he termed "actual neurosis," allegedly resulted from physiological buildup of libido and was manifested by an overwhelming sense of panic accompanied by symptoms of autonomic discharge. In contrast to this form of anxiety, which he did not view as resulting from psychological factors, he observed another variant that originated in a repressed thought or wish and was manifested as a diffuse sense of dread or worry. By 1926, as a result of his tripartite structural model of id, ego, and superego, Freud had further refined his understanding of anxiety. He now viewed it as the result of intrapsychic conflict between aggressive or sexual wishes emanating from the id and complementary responses from the superego in the form of threats of punishment. Anxiety was conceptualized as a *signal* reflecting a danger in the unconscious. In response to this signal, the ego would mobilize defense mechanisms to prevent unacceptable feelings and thoughts from emerging into consciousness. Surprisingly ahead of his time, Freud had already differentiated what we now know as panic disorder from anticipatory anxiety (47, 48).

Elaborating on Freud's early formulations, Nemiah (48) postulated that patients who display symptoms of panic disorder must have an underlying neural structure that can be triggered by psychological and physiological factors. In patients without that neural structure, a milder form of anticipatory or signal anxiety will result.

The neural structure referred to by Nemiah (48) has been further linked to the locus ceruleus by modern neurobiological researchers (49). Dysregulation of γ -aminobutyric acid (GABA) in the locus ceruleus appears to serve as a biologically based etiology of panic disorder (50). Imipramine, which is a highly effective agent in blocking panic attacks, also decreases the firing rate of the locus ceruleus (51). Further evidence of a biological basis for panic disorder includes the induction of panic attacks by sodium lactate infusion in most patients with panic disorder (52), a higher incidence of panic disorder in panic patients' families than in control subjects' families (53), and a 31% concordance for panic attacks in monozygotic twins compared to 0% for dizygotic twins (54).

Although the evidence for neurophysiological factors in panic disorder is impressive, these observations are more persuasive with respect to pathogenesis than to etiology. None of the neurobiological data explain what triggers the onset of a panic attack. In a pilot study in which analysts conducted psychodynamic interviews with nine consecutive patients with panic disorder, an objective research psychiatrist was able to identify mean-

ingful stressors preceding the onset of the panic attacks in every case (51).

Indeed, there are several lines of evidence suggesting that psychological factors may be relevant to panic attacks (1). In the months preceding the onset of panic disorder, patients with the disorder had a higher incidence of stressful life events, particularly loss, than did control subjects (55). Also, in one study (56), 50% of 32 patients with agoraphobia had histories of separation anxiety, and in this group panic attacks often followed the loss of a significant person. In another controlled study of patients with panic disorder (57), the experimental group not only had significantly more life events in the year preceding the onset of panic, but they also experienced greater distress about events in their lives than did the control subjects. The research suggests that panic episodes which appear to be without psychological content and which seem to emerge "out of the blue" may in fact be triggered by *unconscious* psychological factors.

From this perspective, one can argue that the etiology of panic may well involve the unconscious meaning of events, while the pathogenesis may involve neurophysiological factors triggered by the psychological reaction to the events. Busch et al. (51) concluded, "Since each individual interprets the meaning of these events differently, an external stressor may or may not lead to the onset of panic in a neurophysiologically susceptible individual. This suggests that there is a crucial psychological variable that mediates between external events and panic onset" (p. 321).

Some of the most intriguing data regarding panic disorder concern the rate of response to placebo. Anywhere from 25% (58, 59) to 43% (60) of patients with panic disorder show improvement with placebo. These findings are striking when compared to the almost total absence of response to placebo in patients with obsessive-compulsive disorder. Such a dramatic response to placebo is certainly suggestive of psychological factors at work. It may well be that transference factors involved with receiving a pill from a concerned physician work to alleviate the symptoms.

In patients with borderline personality disorder who have not developed the capacity to summon a soothing, holding introject to calm them in times of stress (61), a full-blown panic attack may develop over long weekends when they have no contact with their psychotherapist. Because they cannot evoke an internal image of the therapist, they may begin to fear that the therapist has died or has abandoned them. Under such circumstances, the borderline patient may call the therapist to be reassured by the sound of his or her voice. Hearing just a few words from the therapist over the telephone may immediately terminate the panic attack, as quickly as any pharmacotherapeutic agent.

In this situation, we once again see how neural mechanisms (in the locus ceruleus, in this case) can be influenced as profoundly by psychotherapeutic intervention as by chemical agents. In Waldinger and Gunderson's study of successfully completed long-term psychody-

namic psychotherapy of borderline patients (62), they found that by the fifth year, none of the patients experienced panic in response to their therapist's departures, further evidence suggesting that psychotherapy may produce permanent neurophysiological alterations.

Cognitive-behavioral treatments have also proved effective in the treatment of panic disorder. A recent study by Shear et al. (63) has even demonstrated that lactate induction of panic can be effectively reversed through successful cognitive treatment. These findings, coupled with a variety of case reports of successful treatment of panic disorder with either psychoanalysis or psychodynamic psychotherapy (1, 64-66), provide persuasive evidence that psychological interventions have a major role to play in the treatment of panic disorder.

GENERALIZED ANXIETY DISORDER

The flurry of excitement associated with the significant breakthroughs in panic disorder research have to some extent obscured the continued psychodynamic importance of signal anxiety, as originally described by Freud. This less dramatic variant of anxiety is probably not generated in the locus ceruleus in the same manner as panic disorder (21). Signal anxiety, however neurophysiologically generated, is an enormously informative gateway into the unconscious conflicts residing in the human psyche.

One of the unfortunate consequences of the revised nomenclature in *DSM-III* and *DSM-III-R* is that anxiety is now treated as a disorder in its own right, instead of recognizing that in certain cases it is a signal of unconscious turmoil that deserves investigation. In writing about anxiety from a psychoanalytic viewpoint, Appelbaum (67) referred to it as "a universal, and in that respect normal, phenomenon which may be at any given moment, for any given person, adaptive or maladaptive, too intense or too mild, centered around substitute objects rather than the originally feared ones, an aspect of existential uncertainty or 'neurotic' conviction" (p. 164). The quantitative view of anxiety implies that "less is better." In the assessment of subjects in the Menninger Foundation Psychotherapy Research Project, 18 of 35 patients showed increased anxiety at termination of psychoanalysis or psychotherapy (67). However, 13 of these 18 patients were judged by independent raters to have changed for the better. In evaluating these results (67, 68), the investigators differentiated between primary anxiety, which is disorganizing to the patient (analogous to panic disorder), and anxiety used as a signal. The researchers noted that an increase in tolerance of anxiety, defined as a capacity to experience anxiety without having to discharge it, often occurs as a result of dynamic psychotherapy and reflects expansion of the ego. Many of the improved patients showed a striking capacity to use ideational activity more efficiently in the service of binding anxiety. The investigators concluded that the mere pres-

ence or absence of anxiety after treatment was not sufficient to understand or evaluate change. It may well be that greater ego mastery over anxiety allows one to confront certain existential concerns inherent in life in a more forthright manner.

Anxiety will appear in numerous situations over the course of the life cycle. Whether patients should resort to medication each time they are anxious should be a question of considerable concern to psychiatrists. One can eliminate physiological components of anxiety with medication without addressing the remaining cognitive aspects of the worry. The following vignette is illustrative.

Clinical vignette. Ms. B was a 23-year-old graduate student who came for consultation because of periodic episodes of intense anxiety. About three times a month she would begin worrying about death while lying in bed. Typically, she would start ruminating in the following manner: "I am 23 now; in only 7 years, I'll be 30. Then I'll be 40, and my kids will be grown. Then I'll be a grandparent and retire; and then I'll die." These thoughts led to concerns that her parents, both of whom were alive and well, would soon die. As these thoughts escalated, the anxiety she experienced increased to the point where her heart was racing and she could not fall asleep.

After diagnostic evaluation, I discussed several possible interventions with her: prescription of antianxiety medication, psychotherapeutic exploration of the causes of her anxiety, or a combination of the two. She told me pointedly that she had no interest in medication. "How can a pill make my fear of death go away?" she inquired. She made it clear that she wanted to understand the origins of her anxiety so she could master her fears.

I embarked on a course of psychotherapy with Ms. B that led to increasing ideational mastery over the disturbing affect. I empathized with Ms. B regarding the frightening nature of death, but I noted that concerns about living often contributed to fears about death. I asked her what was going on in her life that might contribute to her anxiety. She immediately replied that it had nothing to do with her husband's being stationed overseas. Tears came to her eyes, and I handed her a box of tissues.

Ms. B ignored the box of tissues and continued talking about how young people were dying of AIDS and cancer. I asked her why she had not taken a tissue when I had offered it to her. She told me she thought it would have been a sign of weakness. I wondered with her if it had always been difficult for her to acknowledge that she needed the help of other people. She responded that all her life everyone had told her their problems, and she could never acknowledge that she had problems and needed help from others. I suggested to her that she might need to present a pseudoindependent facade as a way of denying her neediness. She readily acknowledged that she dreaded the feeling of weakness associated with being vulnerable and needy. I pointed out to her that death was the ultimate situation of vulnerability and neediness. She then responded that the worst thing about death, in her mind, would be having to go through it alone.

As we continued to explore sources of her anxiety, Ms. B revealed a history of having significant difficulties with the expression of anger. She feared that her anger would come out in an explosion that would drive others away from her. Her nighttime anxiety often arose after seeing violent movies. She said it bothered her a great deal that others expressed their

anger in such a violent, forthright manner while she worked so diligently to control hers. Further psychotherapeutic exploration led to the uncovering of a good deal of anger at her father that she had been unable to express. Her unconscious concern was that her anger would be so explosive that it would destroy him.

After 2 months of psychotherapy, the episodes of intense anxiety disappeared. Ms. B still worried about death to some extent, but she had developed greater mastery over the fear as she understood the underlying concerns about the impact of her anger and her fears of being abandoned and alone. In other words, a broadened ideational mastery of the affect enabled her to control her symptoms.

The case of Ms. B illustrates the time-honored principle that in clinical psychiatry we must adapt the treatment to the patient. Contrary to the point of view of some third-party payers, the most appropriate treatment for a patient is not necessarily the most cost-effective. While some clinicians would argue that an antianxiety agent might have more quickly and more cheaply eliminated the patient's symptoms, Ms. B was asking for something other than symptom relief. As Barber and Luborsky (69) have argued, specific anxiety disorder diagnoses require different treatments in different circumstances with different patients. Psychodynamic psychotherapy may be the treatment of choice for the patient who is psychologically minded, motivated to understand the matrix from which the symptom arises, and willing to invest the time, money, and effort in a therapy process. Ms. B did not ask for medication and would probably not have taken it if it had been prescribed.

Disturbing affective states, such as anxiety, are protean in cause and meaning. In some cases anxiety may reflect an apparently random electrochemical burst from the locus ceruleus. In other cases anxiety may serve as a window on unconscious conflict. Following Freud's suggestion of a developmental hierarchy of anxiety, the psychodynamic psychiatrist can explore the specific cognitive correlates of the affect to gain a greater understanding of the origins of the patient's fears. These origins range from the most primitive anxieties—those having to do with disintegration or merger—to more mature concerns about loss of love or castration (1).

CONCLUSIONS

In this communication I have sought to demonstrate the continued relevance of psychodynamic thinking in contemporary psychiatry. A considerable body of research has demonstrated that the human brain undergoes significant functional and anatomical change in response to psychological influences. While this survey has focused on anxiety disorders, similar illustrations of the mutual interplay between the biological and the psychological could be drawn from a myriad of other psychiatric disorders.

To lose the psychodynamic perspective is to lose the

complexity and richness of human functioning in the quicksand of neurotransmitters and molecular genetics. Meaning must be preserved. It is instrumental to the induction of neurobiological changes associated with psychopathology. That which is crucial to etiology and pathogenesis will also be crucial to informed treatment planning. To our great good fortune, mind and brain are inseparable; hence, the "decade of the brain" holds the promise of clarifying their interrelationship.

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Transduction of Psychosocial Stress Into the Neurobiology of Recurrent Affective Disorder

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Early clinical observations and recent systematic studies overwhelmingly document a greater role for psychosocial stressors in association with the first episode of major affective disorder than with subsequent episodes. The author postulates that both sensitization to stressors and episode sensitization occur and become encoded at the level of gene expression. In particular, stressors and the biochemical concomitants of the episodes themselves can induce the proto-oncogene c-fos and related transcription factors, which then affect the expression of transmitters, receptors, and neuropeptides that alter responsivity in a long-lasting fashion. Thus, both stressors and episodes may leave residual traces and vulnerabilities to further occurrences of affective illness. These data and concepts suggest that the biochemical and anatomical substrates underlying the affective disorders evolve over time as a function of recurrences, as does pharmacological responsivity. This formulation highlights the critical importance of early intervention in the illness in order to prevent malignant transformation to rapid cycling, spontaneous episodes, and refractoriness to drug treatment.

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The attacks [of manic-depressive illness] begin not infrequently after the illness or death of near relatives . . . We must regard all alleged [psychic] injuries as possibly sparks for the discharge of individual attacks, but . . . the real cause of the malady must be sought in permanent internal changes, . . . which are innate . . . In spite of the removal of the discharging cause, the attack follows its independent development. But, finally, the appearance of wholly similar attacks on wholly dissimilar occasions or quite without external occasion shows that even there where there has been external influence, it must not be regarded as a necessary presupposition for the appearance of the attack.

—Kraepelin (1)

Unipolar and bipolar affective disorders tend to be not only recurrent but also progressive in the sense that successive episodes occur after shorter intervals of remission, or with increased rapidity of cycling. Approximately 70% of the patients who have a first episode of unipolar affective illness have subsequent episodes, and almost all of the bipolar disorders are re-

current. In a series of studies with large numbers of subjects, which have been reviewed elsewhere (2-4), the median course of illness tended to be characterized by long intervals between early episodes of affective disorders but, with successive recurrences, a progressive shortening of these intervals of remission. While subgroups of patients may show a stable frequency of cycling over time, rapid cycling from the outset, or the more rare variant of "burnout," the tendency for progression appears to be modal across the majority of studies in which the intervals between successive episodes were systematically observed and recorded. These observations have helped to refocus neurobiological theorizing beyond the acute episode to the longitudinal course of affective illness and its tendency for recurrence and progression.

Previously, my colleagues and I (2, 3) have suggested that two preclinical models, behavioral sensitization to psychomotor stimulants and electrophysiological kindling, might provide useful and indirect bridging analogies to help conceptualize various aspects of the neurobiology of the course of affective disorders. This article will focus on accumulating clinical data that suggest the applicability of these models to triggering of episodes by psychosocial stressors and on new neurobiological data that may help conceptualize how this might occur. Thus, the advances reviewed arise in two research realms. Increasing evidence in one area suggests that the first episode of affective disorder, whether it is manic or depressive, is more likely to be associated with major psychosocial stressors than are episodes oc-

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TABLE 1. Studies of Association Between Life Events and First Versus Subsequent Episodes of Affective Disorder

Author	Disorder	Number of Episodes	N	Percent of Patients for Whom Major Life Event Preceded Episode		p	Assessment
				First Episode	Later Episode		
Matussek et al. (9)	Depression	1	242	44		—	Stressors (138 psychological; 58 somatic) had to clearly precede onset of episode
		2	135		34	—	
		3	82		24	—	
		4	119		19	—	
Angst (10)	Depression	1	103	60		—	No inventory
		≥4			38	—	
Okuma and Shimoyama (11)	Manic-depression	1	134	45		—	Any event (3 months prior)
		2	134		26	—	
		3	134		13	—	
Glassner et al. (12)	Manic-depression	1	25	75		—	Event rated stressful by patient and on Holmes and Rahe Scale (1 year prior; usually 2–24 days); role loss critical in patients and comparison subjects
		>1 ^a			56	—	
Ambelas (13) ^b	Mania	1	14	50		<0.01	Paykel Life Events Scale (4 weeks prior); one-third of cases followed bereavement
		≥2	67		28		
Gutierrez et al. (15)	Depression	1	43	55.8		<0.05	Social and somatic stressors; patients with late onset had more events than did those with early onset
		2	35		40.0		
		3	18		38.8		
		≥4	47		29.7		
Perris (8)	Depression	1	37	62	50 ^c	<0.02	Semistructured interview; 56-item inventory (3 months prior)
		≥2	112	43	19 ^d	<0.001	
Dolan et al. (16)	Depression	1	21	62		<0.05	Bedford College-Life Events and Difficulties Schedule (6 months prior) (Brown, Harris, 1978)
		≥2	57		29		
Ezquiaga et al. (17)	Depression	<3	52	50		<0.01	Semistructured interview (Brown, Harris); no effect of chronic stress
		≥3	45		16		
Ambelas (14)	Mania	1	50	66		<0.001	Paykel Life Events Scale (4 weeks prior)
		≥2	40		20		
Ghaziuddin et al. (18)	Depression	1	33	91		<0.05	Paykel Life Events Scale (6 months prior)
		≥2	40		50		
Cassano et al. (19)	Depression	1	94	66.0		<0.05	Paykel Life Events Scale
		≥2	173		49.4		

^aFor this group, the most recent hospitalization was preceded by a life event resulting in role loss.

^bOf surgical comparison subjects, 6.6% had experienced recent major life events.

^cPercentage for negative or undesirable events.

^dPercentage for events involving psychological conflict.

curing later in the course of the illness. The second line of new data arises from recent discoveries in neurobiology indicating how electrical and chemical stimulation and psychosocial stressors affect gene expression and thus present a way in which acute events can have long-lasting effects on the subsequent reactivity of the organism. These data on psychosocial stresses and their potential long-term impact are paralleled by a greatly enhanced understanding of the macro- and molecular biology of sensitization and kindling, thus allowing for more precise conceptualizations of processes that might be pertinent to the longitudinal course of affective disorders.

DIFFERENTIAL IMPACT OF PSYCHOSOCIAL STRESSORS IN FIRST AND SUBSEQUENT EPISODES

A greater role of psychosocial stressors in the initial episode of affective disorder than in subsequent epi-

sodes was observed by early investigators (1, 5–7 [7 also cited in 8]). More recently, systematic studies have explicitly tested and confirmed the notion highlighted in the opening quotation by Kraepelin that there is a greater role for psychosocial stressors in the initial episode than in subsequent episodes. These studies (8–19) are summarized in table 1 and, along with others (20; J. Mendlewicz, personal communication, 1990; M. Thase, personal communication, January 1991; G. Brown, personal communication, September 1991), are noteworthy in that they used a wide variety of measures of the impact of social stressors, ranging from global assessments to detailed systematic measures, such as the Paykel Life Events Scale (13, 14, 18; J. Mendlewicz, personal communication, 1990), the contextual assessment pioneered by Brown and his collaborators (16, 17, 21), and similar in-depth assessments of role loss (12). In the study of G. Brown (personal communication, September 1991), different roles for psychosocial stressors in the first and subsequent episodes were ob-

served only when severe endogenous or agitated depressions, not more minor and neurotic depressions, were included. The National Institute of Mental Health collaborative study on the psychobiology of depression provided data consistent with the current formulation and used a combined census of self- and observer ratings of the impact of psychosocial stressors and their potential role in a given affective episode (20). Patients with an "environment-sensitive" episode had had significantly fewer prior episodes (mean=3.7, SD=4.2, N=28) than those with "autonomous" episodes (mean=13.4, SD=27.4, N=35) ($p<0.05$). Bidzinska (22), Ghaziuddin et al. (18), Perris (8), and Cassano et al. (19) also found more stressors in initial episodes than in subsequent depressions.

It is remarkable that this variety of studies (with the exception of Kennedy et al. [23] and Glassner and Hal-dipur [24]), which had very different methods and assessment instruments, are all consistent in the demonstration that either more psychosocial stressors were involved in the first episode than in subsequent episodes of major affective disorder or psychosocial stressors appeared to have less impact on episodes occurring later in the course of illness, after many recurrences, than on the initial episode. While the majority of these studies were retrospective, the recent prospective study of depressive recurrences by J. Mendlewicz et al. (personal communication, July 31, 1990) also supports this interpretation. Mendlewicz et al. found more psychosocial stressors in association with the emergence of a depressive episode in subjects who had not experienced a depressive episode previously (mean=8.7) than in subjects who had prior histories of unipolar depression (mean=3.9). In the group of subjects without prior episodes, the events in the lives of the subjects who experienced a first depressive episode were more undesirable, negative, and uncontrollable than were the events of those who remained well. Psychosocial stress was thus associated with an initial episode of depression in the normal volunteers but less implicated in the recurrences.

Thus, if we accept the observations in the literature (1, 5-7) and the conclusions from the studies in table 1 (8-19) and others, psychobiological theories must deal with this transition from episodes that are triggered by psychosocial stresses to ones that are less likely to be triggered in this fashion, even though these later episodes occur in the context of increasing vulnerability to recurrence.

KINDLING ANALOGY FOR EVOLUTION TO SPONTANEOUS EPISODES

As previously discussed (2, 3), the kindling model provides an interesting but nonhomologous paradigm (i.e., kindled seizures do not clinically resemble affective illness [25]) in which events that are initially triggered begin to occur spontaneously. Following the development of amygdala-kindled seizures (which occur in response to a stimulation current that was previously

subconvulsant), a sufficient number of repetitions of full-blown seizures will eventually result in the appearance of spontaneous epilepsy, i.e., seizures in the absence of electrophysiological triggers (26-28). Thus, in this "hard-wired" electrophysiological model of amygdala-kindled seizures, there is an evolution from seizures that are triggered by exogenous stimulation to ones that occur autonomously without such stimuli. While the processes underlying the evolution of kindled seizures to spontaneous seizures are likely substantially different from those underlying the progression from stress-engendered to spontaneous episodes of affective disorders, the model presents a clear-cut example of the shift from episodes that are triggered to those that occur autonomously.

Earlier my colleagues and I (3) also discussed the potential relevance of the kindling model in helping to conceptualize processes and mechanisms underlying the initial emergence of robust behavioral phenomena in response to a stimulus that was previously subthreshold. In a parallel fashion, but in different neurochemical systems, repeated stressors (matching events) may come to evoke more robust behavioral consequences than are apparent after the initial stress or loss. While kindling represents a nonhomologous model of affective illness which can be compressed into a time frame of daily evocation of electrical events, kindling can also be elicited by more intermittent stimuli and its persistence (over months to years) fits a time frame pertinent to the affective disorders. Nonetheless, the processes involved in sensitization may be more directly analogous to those occurring in the affective disorders because of the behavioral rather than convulsive endpoints observed.

PROGRESSION OF RESPONSE TO STIMULANTS AND STRESSORS

Psychomotor stimulant-induced and stress-induced sensitization share many elements, and, in some instances, each can produce cross-sensitization to the other (29-34). Stimulant-induced behavioral sensitization also provides a homologous model for the evolution of manic symptoms because many of the progressive components of stimulant-induced mood and behavior mimic the transition from mild and euphoric mania to more severe and dysphoric mania (35) and, ultimately, to full-blown schizophreniform paranoid psychoses (36). While the mechanisms underlying stimulant-induced behavioral sensitization have not been entirely elucidated, it is increasingly recognized that activation of neurotransmitter pathways produces not only acute events associated with rapid alterations in neural firing and short-term neuronal adaptations (37, 38) but also a series of events that have much longer-lasting consequences for the organism. Specifically, the process of neuronal transmission also sets in motion intracellular changes at the level of gene transcription (39-43). One such change is the induction of a series of transcription factors, such as the proto-oncogene *c-fos*,

that subsequently alter gene expression by binding at DNA sites and inducing mRNAs for other substances that may exert effects over long time periods (days to months) (44–48). The transcription factors, such as c-fos and c-jun, are called immediate early genes because of the rapid onset and duration of their effects (minutes to hours). These transcription factors, by virtue of their acute effects, may provide the basis for a spatiotemporal cascade of events that result in more enduring neurotransmitter, receptor, and peptide changes that might provide the biochemical and anatomical basis for long-term synaptic adaptations and memory that could last indefinitely.

EFFECT OF STRESS ON GENE TRANSCRIPTION

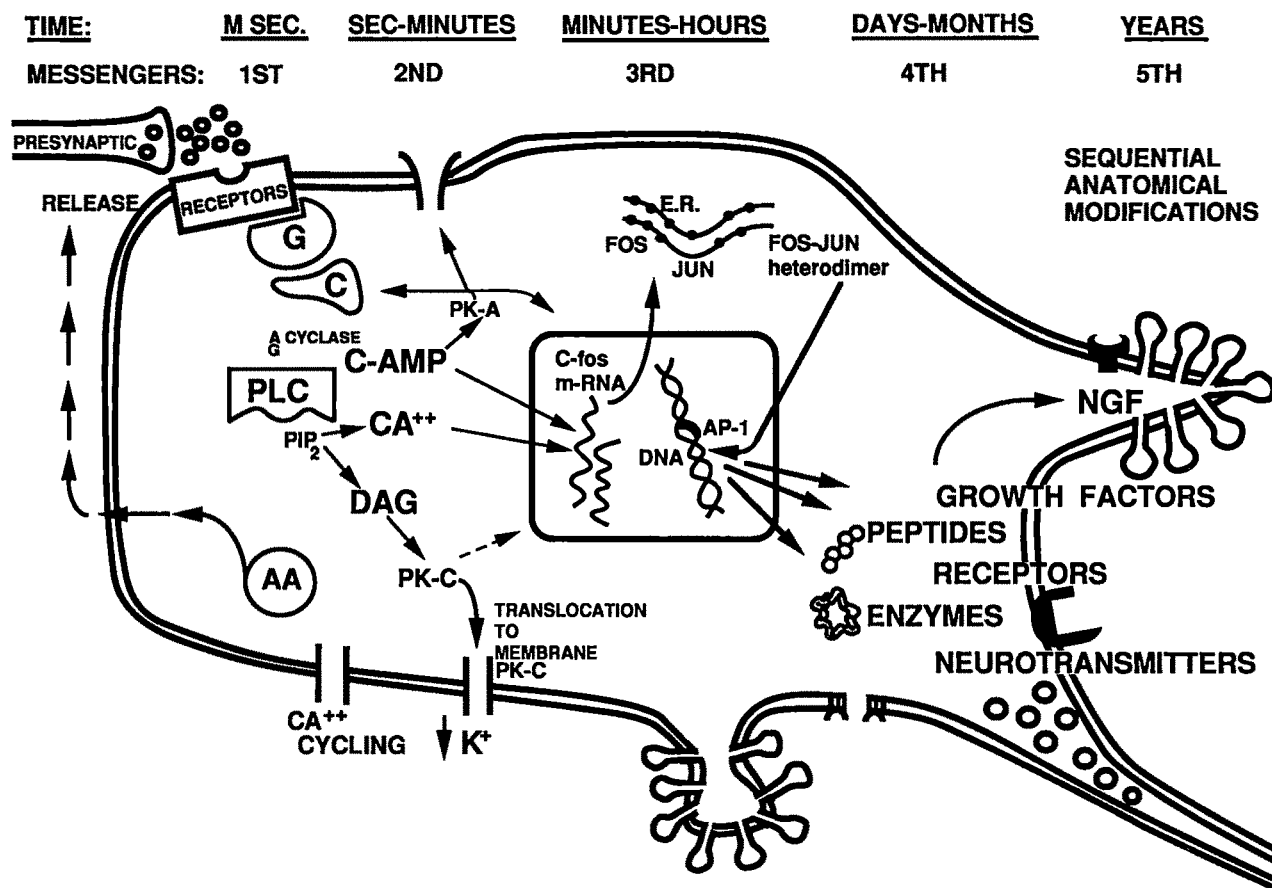
Nakajima and associates in our laboratory (39, 40, 49) and others (42, 50–52) have demonstrated that stresses, even relatively minor ones, are capable of inducing the proto-oncogene c-fos. This can be measured by direct assessment of the Fos protein itself with antibodies (42, 50) or with Northern blot analysis to assess levels of mRNA in discrete tissues (49), or by *in situ* hybridization in which a radioactive probe binds to the mRNA for c-fos in undisturbed structures in brain slices (40, 49). This latter technique has the advantage of providing exquisite anatomical resolution of the areas involved in the c-fos induction (see figure 5 in reference 40). Electroconvulsive seizures administered through ear-clip electrodes to a mouse (40, 49) increase c-fos mRNA expression in the hippocampus, particularly the granule cells of the dentate gyrus, CA1 pyramidal cells, the ventromedial nucleus of the hypothalamus, part of the amygdaloid complex, the piriform cortex, and cerebellum. It is also noteworthy that merely applying the ear-clip for administration of sham electroconvulsive seizures was sufficient to induce low but significant increases in c-fos mRNA in the dentate gyrus, the pyramidal cells of the hippocampus, the piriform cortex, and the cerebellum (49). Even more remarkable is the induction of c-fos mRNA in hippocampal and related areas following the mild stress of an intraperitoneal saline injection. Thus, induction of transcription factors, such as c-fos, occurs rapidly and transiently in a variety of limbic system structures following seizures or even relatively mild stressors.

It is now apparent that a variety of neurochemical systems can induce c-fos in addition to their more direct and classical neurotransmitter functions. Thus, c-fos can be induced by activation of noradrenergic (α_1 , β) (53, 54), dopamine (D_1) (43, 55), acetylcholine (M_1) (56), glutamate (*N*-methyl-D-aspartate) (57), opiate, vasoactive intestinal polypeptide, and nerve growth factor (58) receptors, in addition to induction by the second messengers calcium and cyclic AMP (46, 59).

An important feature of c-fos induction is that it occurs in specific anatomical pathways in the biochemical and physiological systems that are activated. For example, the stress associated with water deprivation in-

creases c-fos in areas of the hypothalamus known to be associated with fluid and electrolyte metabolism (60). Similarly, stress involving nociceptive pathways activates appropriate substrates in the spinal cord and other sites involved in pain (42). Sagar et al. (60, 61) have shown a close parallelism between electrically stimulated cerebellar pathways mapped for metabolic activity by 2-deoxyglucose and those associated with c-fos induction. Moreover, in our laboratory Nakajima et al. (40) and Clark et al. (62–64) have demonstrated that different seizure types are associated with different patterns of c-fos induction. For example, caffeine-induced seizures induce c-fos largely in the striatum and olfactory bulb (65), while those associated with amygdala kindling are more associated with the limbic system, particularly the dentate gyrus of the hippocampus (62, 66). Cocaine-kindled seizures show a pattern involving both striatal and limbic substrates (63). Together, these data indicate the ability of c-fos induction to reflect activation of selective pathways in the CNS (40, 67) and help to address the potential problem of the apparent generality or nonspecificity of c-fos inducibility. Further specificity can be built in by the magnitude and temporal patterning of the expression of multiple transcription factors, as will be discussed.

Most pertinent to the thesis of this article, however, is the possibility that in addition to providing an anatomical marker of pathway involvement, the transient induction of c-fos (lasting several hours) and related transcription factors may also be an initial step in a cascade of neurobiological events that might have long-lasting consequences for the organism. While the long-term effects of c-fos induction have not yet been adequately elucidated, preliminary data from Sonnenberg et al. (68), Morgan and Curran (45, 46), and Crabtree (48) suggest that c-fos induction may be the first step in the induction or suppression of a variety of factors, including peptides, as reflected in the increase in mRNA for prepro-enkephalin that follows c-fos induction. In a correlative fashion, it appears that c-fos induction is sequentially followed by changes in a variety of neurotransmitters, receptors, peptides, and proteins, including nerve growth factors and other substances in the cell (figure 1). In addition, in the development of amygdala-kindled seizures, one can observe the anatomical spread of the putative "memory trace" at the level of mapping of c-fos mRNA. It is initially localized unilaterally in the piriform cortex or dentate gyrus of the hippocampus but becomes bilateral with seizure stage evolution (62). Not only is there induction of the immediate early gene c-fos, but there is also a series of longer-lasting effects on neuropeptides that include alterations in somatostatin (69–72), thyrotropin-releasing hormone (TRH) (73), enkephalin (74–76), and corticotropin-releasing hormone (CRH) (52). There also appear to be long-term decreases in dynorphin (72, 76). While the causal links between transcriptional factor (c-fos) activation and alterations in neuropeptides remain to be directly demonstrated, their temporal sequence of induction (48, 72, 77) and the occurrence in similar anatomical

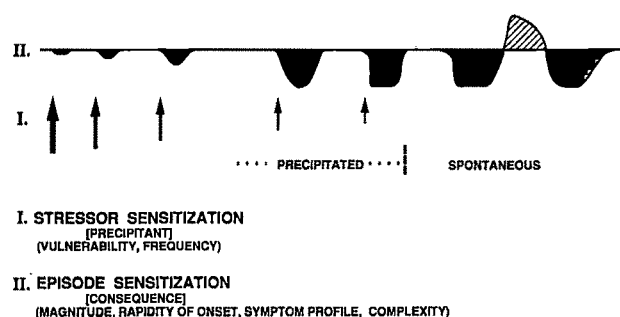
FIGURE 1. Neural Mechanisms of Short- and Long-Term Synaptic Changes Following c-fos Induction^a

^aPLC=phospholipase C, PIP₂=phosphatidylinositol 4,5-bisphosphate, AA=arachidonic acid, DAG=diacylglycerol, PK-C=protein kinase C, AP-1=activator protein—1 (binding site on DNA), E.R.=endoplasmic reticulum, PK-A=protein kinase A, NGF=nerve growth factor.

areas (72) is highly suggestive. It is likely that induction of c-fos, Fos-related antigens, and other transcription factors, such as zif/268, may provide a third-messenger system (78) that then is associated with subsequent changes in gene transcription, providing longer-lasting fourth- and fifth-messenger systems as a result of prior synaptic activation.

Figure 1 illustrates, in a highly schematized fashion, that the time frame of seconds for classical pre- and postsynaptic events in neurotransmission may be only one acute phase of the process and that a variety of other intracellular events occur over much longer time domains. In the 1980s attention focused on longer-lasting but still transient changes in receptor density that occurred as an adaptation to repeated or chronic neurotransmitter exposure. The current conceptual schema suggests that, in addition, a variety of longer-term mechanisms may be brought into play through a cascade of second-messenger systems (79) and changes in protein phosphorylation (that may be involved in long-term potentiation and other types of intermediate memory) as well as the induction of tertiary transcriptional messengers, such as c-fos (45, 48, 60, 68, 78, 80). As illustrated, once mRNA for c-fos is induced, c-Fos pro-

tein is synthesized on the ribosomes of the endoplasmic reticulum. c-Fos can dimerize with itself (homodimer) or form heterodimers with other transcriptional factors, such as c-Jun, which are translocated back into the nucleus to act at AP-1 DNA binding sites that are involved in the initiation of transcription of other proteins, peptides, and growth factors. Fos and Jun interact to form a "leucine zipper" and together bind to DNA in a "scissors grip" fashion (81) more effectively than does either proto-oncogene alone. Fos is only one of many proto-oncogenes (82), and the ratio of Fos to Jun and other Fos-related antigens changes over time (45, 46). This suggests that the oncogene "milieu" conditioned by prior experience may markedly affect the subsequent alterations in gene transcription. In this fashion, specificity and selectivity of responsiveness could be exquisitely regulated according to the prior number, intensity, and "meaning" of prior experiences. Moreover, while c-jun appears to be a positive transcription factor, jun-B appears to have negative or repressive functions, further suggesting that the ratio of oncogenes and other cellular transcription factors can differentially affect the cellular output at the level of long-term changes in gene transcription. In addition to the leucine zipper motif,

FIGURE 2. Two Types of Sensitization in Affective Illness


other oncogenes interact with DNA in other fashions, such as the zinc finger [zif/268(NGFI-A)] and steroid/thyroid receptor homologues (NGFI-B) (81, 82). Complexity and selectivity of response is further suggested by the recent finding that Fos or Jun may interfere with gene induction by the glucocorticoid receptor and vice versa (83, 84). Thus, there appears to be the potential for cross-talk among transcription factors, just as there is for second-messenger systems. Moreover, the interaction between Fos and glucocorticoid receptor elements may take on special importance in the affective disorders, which are characterized by state-related changes in glucocorticoid function.

RELATIONSHIP TO RECURRENT AFFECTIVE ILLNESS

On the basis of the mechanisms just discussed one can draw a fragmentary picture of how psychosocial stressors may come to exert long-term effects on an organism. Type, magnitude, and frequency of repetition of the stressor may be critical to its long-term effects. Elsewhere my colleagues and I (85, 86) have reviewed data indicating that with cocaine-induced behavioral sensitization, the dose of cocaine (perhaps paralleling magnitude of stressors) interacts with the number of repetitions of cocaine administration (paralleling stressor repetitions) to produce an outcome matrix that affects the resulting magnitude and duration of subsequent behavioral responses. For example, repeated low doses of cocaine produce longer-lasting sensitization than does a single high dose. Intermittent doses produce more robust sensitization than chronic, continuous administration.

The quality of the stressor may similarly affect specific neural systems based not only on the type and location of short-term biochemical changes but also on the type, location, mixture, and interaction of oncogenes and transcription factors, with differential consequences for subsequent coding of long-term protein and peptide changes. Psychosocial stresses involving losses and threats of losses in a social context (table 1) may have very different cognitive, behavioral, and neurobiological consequences from stresses involving the threat of bodily injury, which may be more pertinent to the induction of syndromes such as posttraumatic stress

disorder (PTSD). However, some of the same transduction mechanisms discussed here for the encoding of long-lasting alterations at the level of gene transcription may be relevant to the development of PTSD following severe, potentially life-threatening, stressors.

Stressors related to separation, loss, and self-esteem that are associated with the onset of depressive episodes may not only play an important pathophysiological role in the triggering of an affective episode (table 1) but also, because of the neurobiological encoding of memory-like functions related to these stressors, provide a long-term vulnerability to subsequent recurrences and perhaps a mechanism for the retriggering of episodes with lesser degrees of psychosocial stress. In this fashion, one might conceptualize how more minor stresses or losses (and perhaps increasing vulnerability to more symbolic or conditioned stressors and losses) may come to play a role in the triggering of affective episodes. As in the kindling model, with sufficient repetitions of episodes, specific triggers may no longer be required to induce a full-blown syndrome.

Inherent in this concept is the notion that there are two types of sensitization mechanisms—one that is related to the stressor (relating to vulnerability) and another that occurs with the manifestation of an affective episode itself (see figure 2). That is, the experience of an affective episode and its associated neurotransmitter and peptide alterations may leave behind memory traces that predispose to further episodes, i.e., it is possible that “episodes beget episodes.” Cocaine-induced behavioral sensitization perhaps is a relevant model for this process. In this paradigm, animals show increased behavioral responses to repetition of the same dose of cocaine. It is noteworthy that this sensitization process occurs most robustly when cocaine is administered in the same environmental context in which it was previously administered (85–88), suggesting that an associative learning or conditioning component is involved. Fontana et al. (89) have recently demonstrated that this conditioned sensitization is associated with increased dopamine overflow in the nucleus accumbens measured by *in vivo* dialysis in awake, behaving animals, indicating that “psychological” phenomena such as conditioning may have neurobiological concomitants.

Most pertinent to the current argument is the finding that repeated experiences of the behavioral pathology associated with cocaine-induced hyperactivity can engage neural mechanisms that lead to increased rather than decreased responsivity in a very-long-lasting fashion (2, 35, 85, 86). An analogous endogenous process could also occur in recurrent manic or depressive episodes, i.e., the experience of an episode itself (whether or not it is psychosocially triggered) may predispose to greater reactivity or future recurrences. In this regard, it is of interest that cocaine-induced hyperactivity is associated with induction of c-fos, in this instance by a dopamine (D₁) receptor mechanism (41, 43, 55), although it remains to be demonstrated whether c-fos induction is critical to sensitization and its downstream impact on transmitter and peptide (somatostatin, dy-

norphin) regulation. In an analogous fashion, the acute neurotransmitter perturbations of an affective episode potentially involving not only D₁ mechanisms but also acetylcholine, norepinephrine, serotonin, and a variety of other systems (54–58) could, in addition to their acute and intermediate effects on the organism, also leave behind long-term residues (figure 1) as a consequence of c-fos and related transcription factor activation, leading to a cascade of long-term neuropeptide, receptor, and enzyme adaptations. Data of John et al. (90) indicate that the types of memory traces induced in learning may involve changes in the metabolic activity of tens of millions of cells in the brain of the cat, suggesting that the processes outlined in figure 1 could be occurring, in different spatiotemporal domains, in tens of millions of cells as well.

It is also likely that in some instances long-term neurobiological responses to stress may be encoded not only in biochemical processes but also in microanatomical ones. Using an organism as primitive as a snail (*Aplysia*), Kandel et al. (91, 92) have identified anatomical changes at the synapse associated with conditioning. Processes involved in long-term memory build on those used in short-term memory on the basis of an additional impact on gene expression that codes for alterations in synaptic structure as well as function. Nelson and Alkon (93) have documented changes in multiple mRNAs related to associative learning in *Hermissenda*. Even more relevant to the current argument are the recent observations of Rose et al. (94–96) following single-trial passive avoidance learning in the chick. These investigators found that long-lasting learning occurs when a chick is allowed to peck at an attractive, shiny water tube that contains a bitter substance, i.e., it subsequently avoids that tube indefinitely. This avoidance learning is encoded in a spatiotemporally arranged cascade of biochemical and microanatomical effects. These changes include early neurotransmitter and receptor alterations, translocation of protein kinase C, changes in glycogen synthesis, transient induction of c-fos and c-jun, and a variety of other longer-lasting changes that can be identified on a microscopic and electron-microscopic level, including changes in spine density, synapse number and density, and the like. In this paradigm, lesion studies additionally suggest that the gross anatomical location of the putative “memory trace” involved in this learning may (as in kindling) migrate over time, initially involving substrates in the left then right dorsal part of the brain but later localized in ventral parts of the brain, first on the right and then back on the left (96).

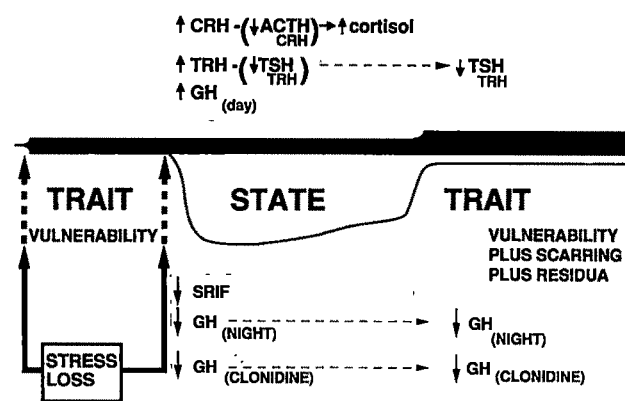
Processes of memory consolidation in the rhesus monkey (97, 98) may also differ as a function of number of learning trials, and they migrate with the passage of time. “Representational memory” may depend on limbic substrates, but “habit memory” becomes independent of these areas and may be based on striatal substrates. An evolution in the macroanatomical structures subserving single versus repeated inductions of behavioral sensitization may also occur. While a single high

dose of cocaine (40 mg/kg) engenders context-dependent sensitization that depends on the presence of the amygdala and nucleus accumbens, three high-dose injections of cocaine result in sensitization that occurs even in the absence of the amygdala (99 and unpublished data of S. Weiss et al., D. Fontana, and A. Pert). Should related mechanisms prove relevant to the neurobiology of affective disorder, they may suggest that, depending on the stage of temporal evolution in the course of affective disorders, not only might the neurochemical and microstructural synaptic mechanisms markedly differ, but the gross neuroanatomical substrates may differ as well. If this proves to be the case, it would support a reconceptualization of the neurobiology of affective disorder as a sequentially evolving process, not a static one. This would have implications not only for therapeutic studies (3) but also for clinical mechanistic studies. It suggests that the neurobiology of affective disorder is a moving target and changes as a function of the longitudinal course of illness.

Again, these conceptual vignettes are presented not with the idea that there are direct behavioral or biological homologies from kindling to the affective disorders, but only with the notion that the kind of long-lasting memory-like processes and their underlying mechanisms may provide a highly preliminary blueprint for parallel alterations in different systems that might occur with a spatiotemporal unfolding pertinent to stress reactivity and vulnerability to affective recurrence. They highlight the multiple levels of spatial and temporal complexity and the major advances in understanding the neurobiology of stress and cocaine sensitization, as well as kindling and related models of long-term plasticity. These models may also begin to provide potential candidates for the types of molecular mechanisms involved in coding the biochemical and anatomical alterations mediating the long-term changes in responsiveness. While findings from these models may be only indirectly relevant to the affective disorders, they highlight principles that may be ultimately applicable to their long-term course and treatment.

IMPLICATIONS FOR THERAPEUTICS

What are the potential implications of such long-lasting changes in both stress responsivity and episode sensitization if one assumes for the moment that the changes outlined here occur and that the details will ultimately be documented? The current formulation emphasizes that modern neuroscience can now incorporate on a more mechanistic basis older psychodynamic theories regarding a critical role of stress and loss in the pathogenesis of affective disorder in some patients. Late in the course of affective disorder, when obvious psychosocial stressors are no longer as apparent as they were earlier, the neurobiological “memory” for this vulnerability to stressors may provide a long-lasting trait marker for the individual. Just as acute seizures (presumably acting through the induction of immediate

FIGURE 3. Progression of State-Trait Phenomenon Over the Course of Affective Illness^a

^aSRIF=somatotropin release-inhibiting factor (somatostatin).

early genes) (47, 49, 62–67) are capable of producing long-lasting alterations in neuropeptides (69–76) and synaptic and neural structures characterized by dendritic sprouting (100), or even cell loss (101), it is postulated that psychosocial stressors, under appropriate circumstances, are likewise able to lead to long-lasting changes in gene expression, including more enduring alterations in neuropeptides (as summarized in figure 3) and even in neuronal microstructure, as demonstrated in other models of learning and memory (91–94). While there is ample evidence for cortisol hypersecretion in depression (perhaps driven by increased secretion of CRH [102, 103]), there is also accumulating evidence for decreases in CSF somatostatin (see reviews by Post et al. [104] and Rubinow et al. [105]). These changes and many others may reflect episode-related alterations in gene transcription (either triggered by stressors or not) that ultimately may deserve direct targeting in therapeutics. However, some alterations may represent changes that are part of the primary pathological process and require amelioration, while others may represent secondary or compensatory attempts at homeostasis and should be augmented (106).

On the basis of the sequentially evolving nature of the affective disorders, we have postulated that the pharmacoresponsivity of the disorder may differ as a function of the stage in its longitudinal course (3, 104), just as it does in kindling and other models of learning and memory. The current formulation also suggests the possibility that different psychosocial and psychotherapeutic interventions may be effective if based on the stage of illness. More specifically, while psychodynamic therapy (perhaps using “representational” or limbic memory systems [97]) may be appropriate for early, minor stress-related dysphorias or initial episodes of major depression, with repeated episodes that begin to emerge spontaneously, use of cognitive, interpersonal, and behavioral therapies may be more appropriate. If the illness is “on automatic,” in part because of many repetitions of episodes, cognitive and behavioral therapies dealing with this automaticity (targeting “habit” or po-

tentially striatal memory mechanisms [97]) may be more fruitful than dynamic therapies.

A critical role for psychopharmacological prophylaxis is also suggested by the current formulation. To the extent that “episodes beget episodes” and repetition of triggered episodes may lead to the occurrence of untriggered ones (see table 1), the dual importance of long-term prevention is reemphasized. Sensitization effects, as well as episodes and their associated morbidity, might be prevented. Biological mechanisms underlying stressor sensitization and episode sensitization in the affective disorders may be conceptualized as having the potential to carry lifelong vulnerability to recurrence.

These neurobiological possibilities square with the clinical data indicating that even several decades of successful lithium prophylaxis does not secure freedom from episode recurrence once the drug treatment is discontinued (4, 107–109). If having an episode increases the risk of subsequent episodes, this variable should be factored into recommendations for earlier initiation and longer maintenance of pharmacoprophylaxis (108). In addition to the liabilities of episode recurrence with the discontinuation of effective prophylaxis, we have identified a small series of patients who initially responded to lithium, relapsed following its discontinuation, but did not re-respond once they were restarted on lithium treatment (109). Thus, it is possible that not only may episodes engender vulnerability to recurrences, but their occurrence may also trigger new mechanisms that can overwhelm or circumvent a previously effective treatment. Similar chemotherapy-resistant processes have been described with the transition from primary-site to metastatic malignancies, which often involve the induction or suppression of additional oncogenes (110–113). Thus, the additional rationale for maintenance of long-term prophylaxis in bipolar disorders to prevent “malignant” transformation to rapid cycling or drug resistance is supported by a modicum of clinical evidence, but it needs to be further documented. Exploration of the potential consequences of failure to maintain prophylaxis is now further bolstered by the initial insights into potential neurobiological mechanisms that may convey these long-lasting vulnerabilities.

In a parallel fashion, the highly recurrent nature of unipolar affective disorder in some patients is increasingly being recognized (3, 4, 114). The long-term prophylactic studies with imipramine (115), fluoxetine (116), and maprotiline (117) not only highlight the high frequency and rapidity of unipolar depressive recurrences within a year after successful treatment of an acute episode (when active drug is replaced by placebo) but also emphasize the effectiveness of prophylaxis in substantially and significantly inhibiting these recurrences (when active drug is blindly continued). The current formulation—that having had an episode leaves behind neurobiological residues that make a patient more vulnerable to subsequent episodes—raises the question of whether earlier institution and maintenance of prophylaxis for unipolar episodes would also decrease the po-

tential for increasingly rapid recurrences, drug refractoriness (virtually unstudied), or chronic depression.

While most studies of the neurobiological concomitants of affective disorders have focused on state-related alterations in classical neurotransmitter, endocrine, and peptide substances, there is increasing recognition that some variables may remain abnormal during the remission between episodes (figure 3). In particular, it appears that a number of patients maintain a blunted thyrotropin response to TRH (118–120), continue to demonstrate sleep abnormalities (121, 122), show abnormal responses in the hypothalamic-pituitary-adrenal axis (123, 124, and F. Holsboer, personal communication), and have blunted sleep-related growth hormone secretion (125, 126). It remains to be documented which of these changes is reliable and which changes are markers of long-term vulnerability to recurrence as opposed to neurobiological “scars” representing markers of having experienced an episode of affective disorder. In either case, the current discussion provides a framework for considering alterations in gene expression as mechanisms by which these changes might arise and in some instances persist.

It is known that in the evolution of some types of cancer there is a long sequence of activation of some oncogenes and loss of other suppressor oncogenes (interacting with environmental influences and hormonal changes associated with development of the organism) which are requisite to the development and progression of tumors (110, 113, 127). This process highlights the potential roles of genetic predisposition, environmental (experiential) factors, and developmental processes (endocrine maturation, etc.) and their interactions (110) in illness evolution. Some of the principles of the development of oncogenesis that have recently been uncovered could be examined for their relevance to the evolution and unfolding of affective illness and its treatment, including the importance of prophylaxis, early intervention, combination therapies, and targeting of therapeutic approaches to the stage of illness.

The clinical data and biological vignettes presented in this article are obviously fragmentary and incomplete, providing only rough landscapes that must be brought into more detailed focus. Nonetheless, they are presented in order to anticipate the more detailed exposition of the precise neurobiological mechanisms involved in different types of learning and memory paradigms and the careful evaluation of their relevance for the longitudinal course of affective disorders. While these developments are eagerly awaited, it may nonetheless be pertinent to begin to formulate questions regarding the nature of the neurobiological changes underlying the longitudinal course of affective disorders so that appropriate studies to explore mechanisms and the impact of psychological and pharmacological interventions can be preliminarily formulated, designed, and tested.

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The Psychotherapist as Witness for the Prosecution: The Criminalization of *Tarasoff*

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The "duty to protect" doctrine heralded by the Tarasoff decision seeks to prevent physical harm to third parties by psychiatric patients. Recent court cases have mandated the testimony of a criminal defendant's psychotherapist both about the Tarasoff warning itself and about confidential treatment information that was associated with the warning. One court further ruled that some clinical sessions were not psychotherapy and therefore were not afforded the protection of psychotherapist-patient privilege. The continuing erosion of confidentiality has resulted in psychiatrists and other mental health professionals becoming prosecution witnesses at the criminal trials of their own patients.

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Prior to the first decision in *Tarasoff v. Regents of the University of California* 1974 (1), psychotherapists faced no legal responsibility to other persons for the future actions of their patients. After embarking upon an unusual rehearing of that case, the California Supreme Court in 1976 issued the definitive *Tarasoff v. Regents of the University of California* decision (2), which enunciated the "duty to protect" doctrine that obligates psychiatrists and other mental health professionals to take appropriate steps to diminish the danger posed by their patients to certain third parties. Failure to discharge that duty properly, coupled with a subsequent injury to the threatened person, exposes the therapist to civil damages for malpractice. In a previous article in this journal, Mills et al. (3) recounted the details of the *Tarasoff* case and its many progeny in other jurisdictions over the ensuing decade.

In California the *Tarasoff* duty to protect can be fulfilled by any clinical intervention designed to reduce patient dangerousness, including inpatient or outpatient

treatment by pharmacologic, behavioral, and/or psychotherapeutic means. If clinical interventions are not deemed sufficient, the psychotherapist can breach confidentiality and alert the potential victim through a "Tarasoff warning." Since violence perpetrated by patients is not always preventable, the existence of a duty to protect serves as a continuing source of anxiety for the malpractice-conscious psychotherapist. Further, a patient could conceivably file a civil suit against the therapist for breaching confidentiality by warning a potential victim. A difficulty associated with duty to protect doctrines in states such as California is that the legal rules arise from case law and not statutory law enacted by the legislature. Case law, as elaborated through judicial decision, is oftentimes predicated solely on the unique facts of a particular case and may prove difficult to apply in other instances. In response to these concerns, several states have adopted statutes protecting psychotherapists from civil liability for harm inflicted by their patients if certain legally prescribed steps are taken (4). In California, for instance, psychotherapists must warn both the foreseeable victim and the police in order to enjoy protection from subsequent lawsuits (5).

Despite the widespread attention that the duty to protect and its attendant breach of confidentiality have received (6, 7), psychiatric commentators have not anticipated the use of a *Tarasoff* warning as a potent prosecutorial weapon during subsequent criminal proceed-

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ings against a patient. In three recent murder cases, *People v. Clark* (8), *People v. Wharton* (9), and *Menendez v. Superior Court* (10), California courts have significantly eroded the concept of patient confidentiality and the enterprise of psychotherapy by opening psychiatric treatment to public scrutiny after the danger posed by the patient/defendant had ended.

In modern times, the patient generally has the prerogative of deciding when and with whom the contents of the psychiatric record can be shared. Related to this prerogative is (testimonial) privilege. Privilege is statutory law granting the holder of the privilege the right to prevent the person to whom confidential information was given from disclosing it in a legal proceeding (11). The California psychotherapist-patient privilege statute provides for the confidentiality of psychotherapist-patient communications in order to safeguard the therapeutic process (12). Interestingly, part of the legal rationale behind the *Tarasoff* duty involves the "dangerous patient" exception (13) to the psychotherapist-patient privilege, despite the fact that the *Tarasoff* situation did not involve a legal proceeding. All three of the cases we discuss here relied heavily on this dangerous patient exception to allow introduction of a *Tarasoff* warning as evidence into a criminal proceeding. This statute reads, "There is no privilege . . . if the psychotherapist has reasonable cause to believe that the patient is in such mental or emotional condition as to be dangerous to himself or to the person or property of another and that disclosure of the communication is necessary to prevent the threatened danger." We present brief summaries of each of these landmark cases, followed by an explanation of the implications of this legal assault on the practice of psychiatry.

CASES

People v. Clark

Mr. Clark was charged with capital murder after being accused of setting fire to the home of his former psychotherapist, causing her to suffer substantial burn injuries and causing her husband's death. A defendant convicted of capital murder faces either the death penalty or life in prison without the possibility of parole.

Defense counsel retained a clinical psychologist, among other expert witnesses, to assist in the evaluation of Clark's mental status for possible use in his defense. The clinical psychologist was confidentially retained under both the attorney-client privilege and the psychotherapist-patient privilege. During the psychological assessment, Clark told the clinical psychologist of his plan to kill two individuals—one who he believed had caused the dissolution of a previous marriage and the other who he believed had encouraged his former psychotherapist to terminate his psychotherapy. Several months later, the clinical psychologist discharged her perceived *Tarasoff* duty by having her attorney notify the identified potential victims.

Clark was eventually convicted of capital murder. During the penalty phase of the trial to determine Clark's sentence, the trial judge permitted the clinical psychologist to testify about Clark's homicidal threats. The judge allowed the *Tarasoff* warning into evidence on the basis of the dangerous patient exception to the psychotherapist-patient privilege. The judge ruled that Clark had waived his privilege by expressing the threats. Although the trial judge did not rule that Clark had waived his attorney-client privilege, the judge nevertheless accepted the clinical psychologist's testimony about the *Tarasoff* warnings. Clark subsequently received the death penalty.

On appeal, the California Supreme Court affirmed the death sentence. While the admissibility of the *Tarasoff* warnings as prosecutorial evidence was not central to the Court's legal decision, the justices did opine that once confidential information is disclosed to others (in this case, to the identified potential victims) in a non-privileged communication, it forever loses its confidential status. The Court did, however, agree with the defense contention that since the attorney-client privilege had not been waived, the *Tarasoff* warnings had been wrongly admitted into evidence. However, the Court felt that this error had only a negligible effect on the outcome, was therefore not prejudicial, and did not justify a rehearing.

People v. Wharton

Mr. Wharton and Ms. S had been cohabiting for about 1 year when Mr. Wharton sought treatment from a postdoctoral psychology intern and a psychiatrist for his anger and fear of physically harming Ms. S. During his second session with the psychologist, Wharton agreed to bring Ms. S to the next scheduled meeting in order to discuss his violent thoughts about her. Nonetheless, the psychologist telephoned Ms. S and issued a *Tarasoff* warning, telling her that she was in danger and should stay away from Wharton. Although Ms. S had previously been physically attacked and threatened by Wharton, she said that she feared being lonely and felt that if she left, Wharton would kill her anyway. About 1 week after the fourth psychotherapy session with the psychologist, Wharton killed Ms. S in their apartment.

At issue in Wharton's trial was whether the prosecutor could prove the elements of premeditation and deliberation that are needed for a first-degree murder conviction. Over defense objections, the trial judge permitted the psychologist and the psychiatrist to testify about the information obtained during their treatment of Wharton that led them to issue the *Tarasoff* warning. The judge ruled that the dangerous patient exception to the psychotherapist-patient privilege applied and permitted the psychotherapists to testify about the *Tarasoff* warning process, including all information related to the warning. In fact, the defendant's psychotherapists had joined in the prosecution's petition to be allowed to so testify.

The jury returned a verdict of capital murder. During

the sentencing phase, the prosecution relied heavily on the testimony of Wharton's psychotherapists to support the argument in favor of the death penalty, with which the jury unanimously agreed.

On appeal, the California Supreme Court affirmed the death sentence by a 4-to-3 vote. The four-justice majority found no violation of the psychotherapist-patient privilege, since the confidential communications were deemed to have become nonconfidential as a result of the *Tarasoff* warning. The Court also allowed into evidence the confidential information on which the psychotherapists based their decision to provide the *Tarasoff* warning, even though this material was not directly a part of the *Tarasoff* warning.

In *Wharton*, three California Supreme Court justices offered two separate dissenting opinions. The first argued that the majority had incorrectly interpreted the dangerous patient exception statute by ignoring the intent of the statute to avert future harm in using it to cover a danger that had already passed. The second dissenting opinion objected to the enormous discretion that the majority opinion afforded the state in introducing information beyond the confines of the *Tarasoff* warning. Prosecutors could henceforth admit into evidence all "impressions and diagnoses which prompted such warnings . . . [and] . . . statements made by the defendant himself which lead to impressions, diagnosis and conclusions by [the psychotherapists] to warn the victim." Both dissenting opinions stated the belief that a retrial was indicated because without prosecutorial use of either the *Tarasoff* warning (first dissenting opinion) or excessive amounts of confidential information beyond the *Tarasoff* warning (second dissenting opinion), the prosecution might not have been able to prove that Wharton had formed the requisite mental states (i.e., premeditation and deliberation) for first-degree murder.

Menendez v. Superior Court

Two brothers, E. Menendez and J. Menendez, were accused of murdering their parents. A couple of months later, on Oct. 31, 1989, E. Menendez met with the clinical psychologist who was treating both brothers. Because the psychologist sensed that E. Menendez might wish to confess to the killing of his parents, he arranged for his business associate, Ms. S, to be nearby so that she could call the police if trouble arose. E. Menendez stated that he and his brother had killed their parents. Fearing that J. Menendez was the more dangerous of the two brothers, the psychologist telephoned him and invited him to his office to determine his response to his brother's revelation. The psychologist asked Ms. S to eavesdrop on that session.

As a result of the Oct. 31 session, the psychologist concluded that he and his family were in danger. He telephoned his wife and told her that his patients had confessed to having killed their parents and instructed her to take their children and leave home. He also feared that Ms. S was in danger.

The psychologist concluded that the best way to reduce the danger to himself, his family, and Ms. S was to convince his patients that he was their ally and that if they continued to see him, the information they revealed "could potentially be helpful . . . in the event they were brought to trial for their parents' murder." For his own protection, he audiotaped the ensuing three sessions. On Nov. 2, he told the brothers that although the session was confidential, if they threatened him or anyone else, or if anything happened to him, the tapes would be given to the police. The majority of the third session was devoted to a discussion of E. Menendez's fear of his brother. The fourth session focused on the brothers' "family constellation," including their relationships with each other and with their parents.

During the first week of March 1990, after the psychologist and Ms. S had ended their association, Ms. S went to the police and revealed everything she had learned about the brothers. Using this information, the police obtained a search warrant for the audiotapes.

Defense counsel sought to prevent the admission into evidence of the communications to the psychologist during the four audiotaped sessions. The trial judge ruled that the contents of these four sessions were not confidential because the psychologist had made reasonable and necessary disclosures pursuant to the dangerous patient exception to the psychotherapist-patient privilege after the session of Oct. 31, 1989. On appeal, in a unanimous decision, the California Court of Appeal extended the trial court's ruling by holding both that the contents of the first two sessions were rendered nonprivileged by the dangerous patient exception and that the final two sessions were not in fact psychotherapy, so the psychotherapist-patient privilege could not apply.

DISCUSSION

In all three cases, the prosecution's access to the once-privileged and confidential psychiatric record began with a *Tarasoff* warning. In essence, once confidentiality is lost in one context, it can never be regained in another.

Clark was the first case that delineated the basis for the erosion of the psychotherapist-patient privilege. Although the psychologist had properly carried out her *Tarasoff* duty by a warning, the California Supreme Court held that its admission into the trial had been in error because it violated the attorney-client privilege under which the psychologist had also been appointed. However, this violation of confidentiality was not considered legally important to the outcome. Despite the aforementioned court viewpoint being "dicta" (expressions in the court's opinion which go beyond the facts before the court and therefore are individual views of the author of the opinion and not binding in subsequent cases [14]), the threat inherent in the *Clark* ruling lay in the likelihood that the use of a *Tarasoff* warning during trial would extend to nonforensic, clinical settings (15),

as has now been realized in the subsequent *Wharton* and *Menendez* rulings.

Wharton is important to psychiatrists and other mental health professionals because it expands the scope of confidential information that could be revealed during a trial. *Wharton* permits the courtroom disclosure of all confidential psychotherapist-patient communications that were considered by the therapist in reaching the decision to issue a *Tarasoff* warning. It can be exceedingly difficult to determine what previously confidential psychotherapist-patient information formed the basis for a *Tarasoff* warning. A psychotherapist's countertransference toward a patient who has committed a heinous crime could affect how he or she retrospectively perceives the scope of material that led to the warning. It can only be speculated what the reasons were that prompted *Wharton*'s psychotherapists to join in the district attorney's petition to allow them to testify.

A prominent concern generated by *Tarasoff* has been whether potentially violent patients would be dissuaded from seeking treatment and participating openly in sessions (16). The *Wharton* case further heightens this concern by raising the specter of the psychotherapist serving as a prosecution witness. The California Supreme Court in its majority opinion dismissed this concern as "entirely speculative." Instead, it considered public safety as its priority, citing Justice Tobriner's often-quoted comment in *Tarasoff* that "the protective privilege ends where the public peril begins." However, the *Tarasoff* danger from *Wharton* ended when Ms. S was killed.

A question that remains unanswered is how a potentially violent patient would react to the knowledge that his or her psychotherapist could become a prosecution witness. The *Menendez* case raises fears for clinicians' safety when confidentiality is breached by implementing the *Tarasoff* duty. The Appellate Court's consideration of *Menendez* was conducted independent of the Supreme Court's review of *Wharton*. What might the *Menendez* brothers have done to their therapist if *Wharton* had already been decided and they knew that their sessions would be disclosed in court?

The *Menendez* decision does not appear to lead to erosion of psychotherapist-patient confidentiality beyond that of *Wharton*. However, a noteworthy intrusion on psychiatric practice is the *Menendez* Appellate Court's determination of what constitutes psychotherapy. While the original *Menendez* court was concerned only with ruling whether confidentiality afforded by the psychotherapist-patient privilege applied to the sessions, the Appellate Court established new ground by deciding which sessions were actually psychotherapy and which were not. Such a judicial determination goes far beyond the province or knowledge of the judiciary by transgressing professional boundaries and failing to recognize the unique expertise of mental health professionals in conducting their work.

These three cases suggest that a *Miranda*-type warning, informing the patient of the existence of the *Tarasoff* duty and its potential consequences in future criminal proceedings, might be advisable when one treats

certain violence-prone patients. While *Miranda*-type warnings appear to offer a straightforward legal solution (17), ethical and clinical pitfalls remain (18).

The *Tarasoff* warning has assumed a novel legal role beyond its original intent as a single intervention designed to safeguard an endangered third party. Accordingly, determining the appropriate uses of this warning merits serious consideration. A possible approach might be for legislative action to limit or prohibit the admission into evidence in criminal trials of a *Tarasoff* warning and any related clinical material in those jurisdictions where a *Tarasoff*-type duty to protect exists. Legislative remedies to define more precisely the *Tarasoff* duty are not without debate and concern within the psychiatric profession, as they raise questions regarding the potential misuse of psychiatry to achieve social control (19, 20). Nevertheless, placing the psychotherapist in the predicament of possibly becoming a witness for the prosecution, particularly in death-penalty cases, places nonforensic psychotherapists in a precarious ethical bind. Even forensic psychiatrists accustomed to these issues have been divided over the ethical propriety of participating in capital cases, especially in the role of expert witness for the prosecution (21).

While the specific cases discussed in this article were all capital cases, their applicability in California law reaches all criminal cases. Beyond California's borders, the possibility of the prosecution's use of a *Tarasoff*-type warning in a criminal trial depends on local law. However, there is no reason to believe that the general legal principles underlying these California cases cannot be adjudicated elsewhere.

Psychiatrists and other mental health professionals, through their respective professional organizations, may wish to adopt a proactive policy of advocacy in the legislature for statutory limits on the prosecutorial use of the *Tarasoff* warning and related clinical material. In the absence of such efforts, psychotherapists will continue to be called as prosecution witnesses, with a resulting threat to their safety. Finally, the tension associated with these possibilities will likely further distance psychotherapists from treating difficult and dangerous patients. It may be acceptable to warn potential victims in an attempt to avert tragedy, but it may well prove intolerable for therapists to assume a prosecutorial role long after the danger has dissipated.

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Decreased Brain Metabolism in Neurologically Intact Healthy Alcoholics

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***Objective:** The extent to which cerebral dysfunction in alcoholics is related to the direct effects of alcohol in the brain rather than to indirect mechanisms and/or alcohol withdrawal remains unclear. The purpose of this study was to evaluate whether healthy alcoholics with no evidence of alcohol-associated complications showed changes in brain glucose metabolism. **Method:** Positron emission tomography and [^{18}F]-fluorodeoxyglucose were used to measure regional brain metabolism. The study group consisted of 22 normal, healthy, right-handed volunteers and 22 neurologically intact, healthy, right-handed alcoholics tested 6 to 32 days after alcohol discontinuation. **Results:** Alcoholics showed significantly lower whole brain metabolism than normal control subjects. Normalization of regional metabolic values to the whole brain metabolic rate revealed that the left parietal and right frontal cortices were the most affected regions. Although the whole brain metabolic rate was correlated with the amount of time since alcohol discontinuation, the "normalized" decreases in left parietal and right frontal glucose metabolism were not. **Conclusions:** These findings support the contribution of the direct effect of alcohol as well as alcohol withdrawal on the changes in regional brain metabolism seen in alcoholics. They also provide evidence of cerebral changes in neurologically intact healthy alcoholics.*

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Chronic excessive ingestion of alcohol is associated with cerebral dysfunction as indicated by electrophysiological (1, 2), neuropsychological (3, 4), neuro-radiological (5-11), and nuclear imaging (12-21) studies. However, the extent to which the cognitive deficits in alcoholics stem from factors other than alcohol, such as trauma, abnormal nutrition and metabolism, and/or alcohol withdrawal, is unclear (22).

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Measurements of cerebral blood flow (CBF) and of brain glucose metabolism have been shown to be sensitive indicators of cerebral function (23). Multiple studies have been done to evaluate changes in CBF in chronic alcoholics (15, 18). Although there are discrepancies among investigators, most studies tend to report decreased CBF in alcoholics. The extent to which CBF changes in alcoholics reflect changes in brain function is confounded by the direct vasoactive properties of alcohol (24), which could lead to uncoupling of energy metabolism and CBF. Studies done to directly evaluate changes in brain energy metabolism in alcoholics have shown mixed results. Two positron emission tomography (PET) studies in alcoholics (19, 20) have revealed decreased brain glucose metabolism, but another study (21) revealed no such change. The disparate results reported could reflect differences in the status of the patients and/or differences in how long after alcohol withdrawal the studies were done.

The purpose of this investigation was to assess regional brain glucose metabolism in neurologically intact, medically healthy alcoholics and its relation to alcohol withdrawal. Since this investigation was carried out with two different PET cameras, a separate set of

TABLE 1. Characteristics of 22 Normal Subjects and 22 Alcoholics Studied With PET VI and CTI

Characteristic	PET VI Study				CTI Study			
	Normal Subjects (N=11)		Alcoholics (N=11)		Normal Subjects (N=11)		Alcoholics (N=11)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (years)	36	6	38	3	32	12	39	7
Education (years)	16	3	14	2	15	3	13	1
Duration of heavy alcohol use (years)			21	3			24	7
Duration of alcohol withdrawal (days)	>6		11	3	>6		17	6
IQ	—		105	3	115	3	106	10

scans of normal control subjects was run for each camera and the results are reported separately.

METHOD

Alcoholic Subjects

The group of alcoholics consisted of 22 right-handed men who fulfilled *DSM-III-R* criteria for alcohol dependence. The patients' ages ranged from 28 to 51 years, and they all had at least a 15-year history of alcohol abuse. The patients were from a Veterans Administration (VA) detoxification unit and had been detoxified 6 to 32 days before the study. At the time of admission, patients were withdrawn from alcohol with decreasing doses of chlordiazepoxide over a 72-hour period and remained in the hospital throughout the evaluation. A complete physical, psychiatric, and neurological examination, including clinical laboratory evaluation (cell blood count, blood chemistries, liver function tests, thyroid screen, urine analyses) and urine drug screen were performed to rule out medical illness and/or use of psychoactive drugs other than alcohol. All of the patients had a positive family history of alcoholism in at least one of their first-degree relatives and had an early-onset history of alcoholism.

Exclusion criteria were past or present history of drug abuse other than alcohol, past or present history of medical or neurological diseases, past or present history of psychiatric illness other than alcoholism (special emphasis was placed on excluding comorbidity with psychoses or affective illnesses; patients with scores on the Hamilton Rating Scale for Depression above 15 were excluded), past history of hepatic encephalopathy, and current seizures, delirium tremens, need of psychoactive medication (other than chlordiazepoxide), and malnutrition (body weight less than 20% of ideal body weight). Chlordiazepoxide was discontinued at least 6 days before the PET study, and PET studies were delayed until there was no evidence of signs or symptoms of withdrawal.

Normal Control Subjects

Twenty-two right-handed male volunteers 23–59 years-old were recruited for this study. They were given

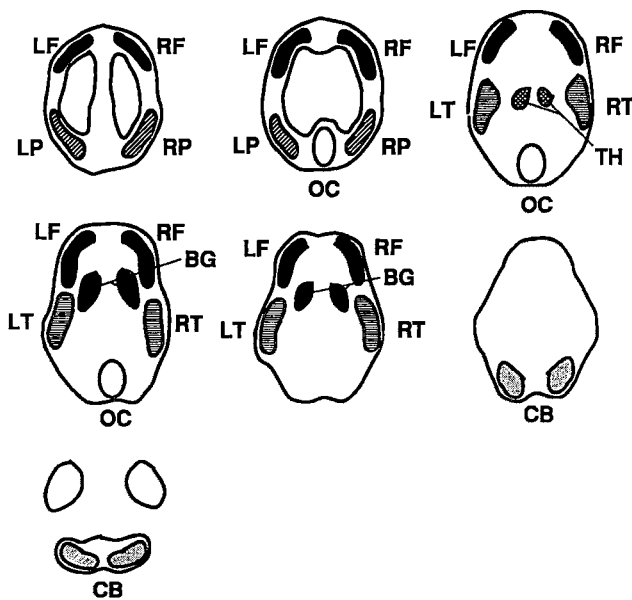
the same evaluation as the alcoholics to ensure absence of medical illness. Urine screens for toxicology were performed twice during the week of the PET scan to ensure lack of use of psychoactive substances. Prospective control subjects were excluded if they had a past or present history of psychiatric, neurological, or medical disease, required medication, had a history of head injury, had a past or present history of alcohol or drug abuse, or had a first-degree relative who was alcoholic. Subjects' use of alcohol was quantitated for frequency of use, dose consumed, and pattern of use. Subjects who used alcohol only under social situations, not more than once a week, without use leading to alcohol intoxication, and not more than 4 g of alcohol per week were included in the control group. None of the alcoholic or normal control subjects were receiving any type of medication at the time of the study.

Half of the normal control subjects and half of the alcoholics were scanned by using the PET VI, and the other half were scanned by using the CTI tomograph. Table 1 provides demographic and clinical characteristics of the subjects for studies on the two tomographs.

All subjects received a neuropsychological examination. In addition, the normal control subjects and the alcoholics studied with the CTI received an magnetic resonance imaging (MRI) scan done on a GE Signa 1.5 Tesla system to exclude those with substantial structural brain abnormalities (subjects with evidence of moderate or severe cortical atrophy/and or ventricular enlargement were eliminated from the study). The MRI scans were rated blindly by three independent investigators for rate of cortical atrophy and for ventricular enlargement (0=none, 1=mild, 2=moderate, 3=severe) (interrater reliability $r=0.96$).

Scanning

The PET scans were performed for one of the studies on the PET VI tomograph in the high-resolution mode (in-plane resolution of 9 mm, full width half maximum) and for the other study on a CTI tomograph (model 931) (in-plane resolution 6 mm, full width half maximum). The PET scans were performed following an intravenous bolus injection of 5–7 mCi of [^{18}F]-fluorodeoxyglucose (FDG). All scans were done under baseline conditions (eyes open, ears unplugged) in a dimly lit room with noise kept to a minimum. Positioning of the

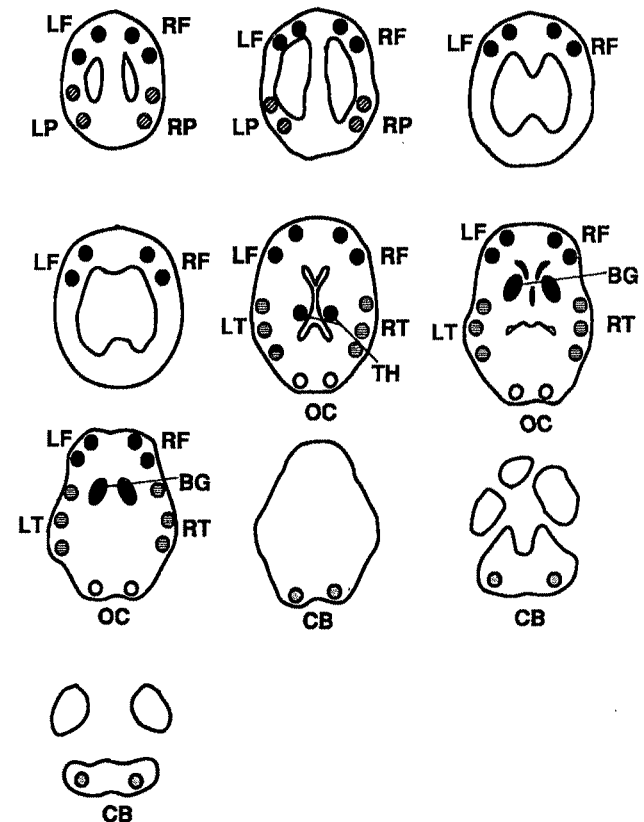
FIGURE 1. Location of Regions Sampled to Obtain Metabolic Values for 10 "Composite" Brain Regions From PET VI Images^a

^aMetabolic values of regions of interest corresponding to the same anatomical areas (shaded similarly) were averaged to obtain "composite" values. Composite values for left (L) and right (R) frontal (F), parietal (P), and temporal (T) cortices were obtained, and one value was obtained for occipital cortex (OC), thalamus (TH), basal ganglia (BG), and cerebellum (CB).

subject in the gantry was accomplished by using an individual headholder and two sets of weak laser fan beams that illuminated the head surface along the canthomeatal line and along the sagittal line, respectively. Before radiotracer injection, each subject underwent a transmission scan performed with a ring filled with germanium 68/gallium 68 to allow the subsequent emission image to be corrected for attenuation. A catheter was placed in the antecubital vein for radiotracer injection and in a dorsal hand vein for "arterialized" blood sampling (25). Arterialized blood was obtained to measure FDG, glucose, PO₂, and PCO₂. The PET scans were taken 35 minutes following injection of FDG. For the study done on the PET VI the scans were done for a total of 8 minutes; the CTI studies were carried out for 20 minutes. Metabolic "rates" were calculated as described elsewhere (25). Studies followed the guidelines approved by the human studies research committee at both our laboratory and the VA medical center, including informed consent procedures.

Image Analyses

Regions of interest were drawn directly on the PET images by using the Matsui/Hirano atlas as a reference (26). Thirty-four regions of interest were selected from the images obtained with the PET VI, which provides seven contiguous slices. Seventy-two regions of interest were selected from 10 of the 15 images obtained with

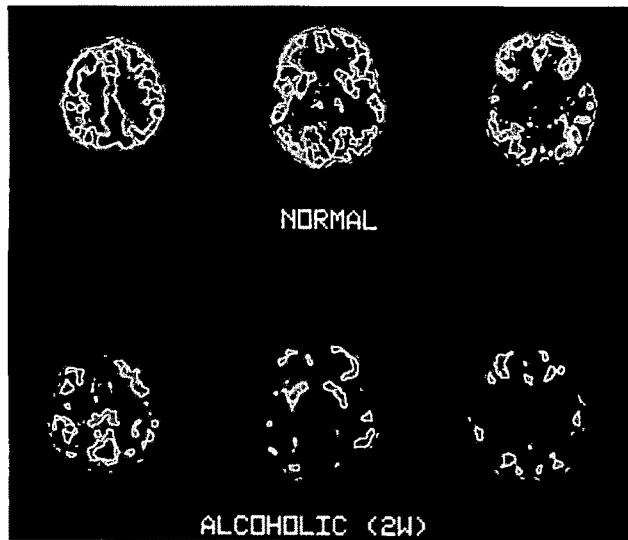
FIGURE 2. Location of Regions Sampled to Obtain Metabolic Values for 10 "Composite" Brain Regions From CTI Images^a

^aMetabolic values of regions of interest corresponding to the same anatomical areas (shaded similarly) were averaged to obtain "composite" values. Composite values for left (L) and right (R) frontal (F), parietal (P), and temporal (T) cortices were obtained, and one value was obtained for occipital cortex (OC), thalamus (TH), basal ganglia (BG), and cerebellum (CB).

the CTI. Weighted averages (to correct for difference in sizes) of the regions of interest from different slices corresponding to the same anatomical areas were computed to obtain metabolic values in 10 "composite" brain regions. Figures 1 and 2 show the location of the regions of interest sampled and the regions of interest that were included to obtain the 10 "composite" brain regions for the PET VI and for the CTI images, respectively.

A mean value of whole brain glucose metabolic rate was obtained by averaging the metabolic rates from all the pixels within the skull. "Relative" measures of regional brain metabolism were obtained by using the ratio of the metabolic value in the "composite" brain regions to the metabolic value for the whole brain. Differences in absolute and relative brain glucose metabolism for the "composite" brain regions between normal control subjects and chronic alcoholics were analyzed by using two-tailed Student's *t* test separately for the studies done on both tomographs. Because of the multiple comparisons involved in the analyses, differences were considered significant only if they were

FIGURE 3. Brain CTI Metabolic Images in a Normal Control Subject and an Alcoholic Subject Tested 2 Weeks (2W) After Last Use of Alcohol^a



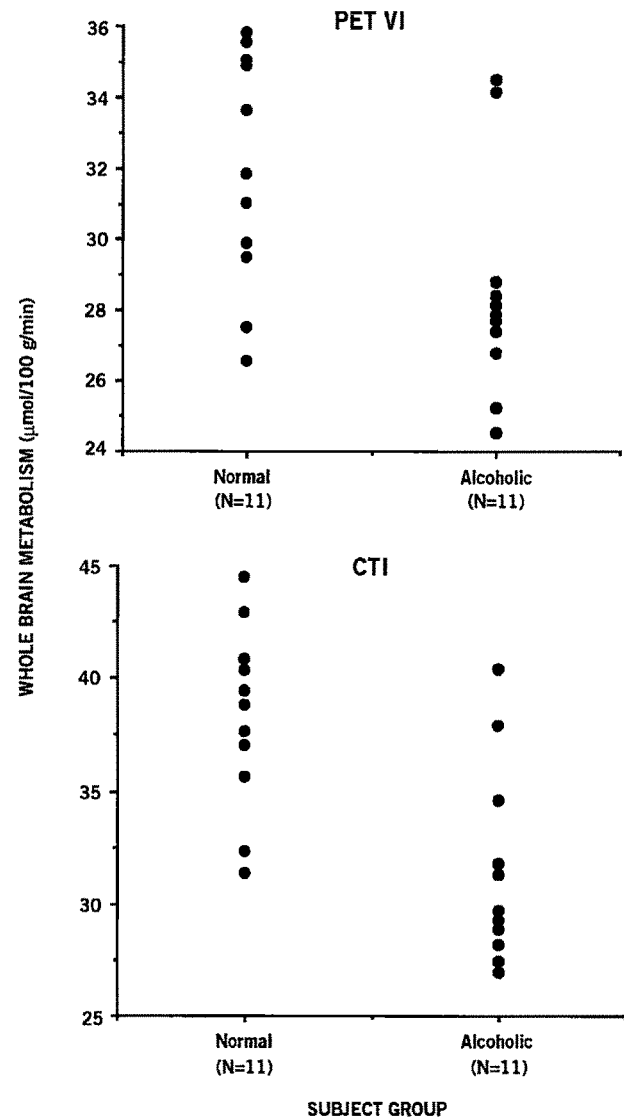
^aNotice the decreased cortical metabolic activity in the alcoholic.

significant ($p < 0.05$) in both studies. Since the normal control subjects were younger (mean=32 years, SD=12) than the alcoholic patients (mean=39 years, SD=7) in the study done with the CTI, the effect of aging on brain metabolism was evaluated in this group of subjects by obtaining the regression equation for global brain metabolism and age in the normal control subjects and then obtaining the predicted metabolic values for subjects of that age among the alcoholics. The differences between the observed and the predicted metabolic values were then tested for significance with one-sample two-tailed t tests. This analysis was used because the covariate analysis was inappropriate due to differences in the regression lines between normal subjects and alcoholics. To evaluate the contribution of alcohol withdrawal to the metabolic changes found in the alcoholic subjects, we performed a correlational analysis between the variables that were found to be significantly different between normal subjects and alcoholics and the days since last alcohol use.

RESULTS

Neuropsychological evaluation of the alcoholic subjects did not reveal evidence of major cognitive impairment in these patients. The only tests on which alcoholics performed significantly worse than normal subjects were the Trailmaking test (27), the Symbol Digit Modalities (28), and the Stroop (29). The 11 alcoholics for whom MRI scans were obtained showed evidence of mild cortical atrophy (mean=1.1, SD=0.7) and mild ventricular enlargement (mean=0.9, SD=0.8), but the 11 normal subjects for whom scans were obtained did

FIGURE 4. Individual Values for Whole Brain Metabolism of Normal Subjects and Alcoholics Studied With PET VI and CTI



not (cortical atrophy mean=0.2, SD=0.5; ventricular enlargement mean=0.3, SD=0.05).

Alcoholics had significantly lower whole brain metabolism than normal control subjects. Figure 3 shows the brain metabolic image for a normal control subject and for an alcoholic, and figure 4 shows the individual values for whole brain metabolism for the normal subjects and for the alcoholics. The two studies showed whole brain metabolism to be significantly lower in alcoholics. For the PET VI study, normal subjects had a mean of 31.8 $\mu\text{mol}/100 \text{ g/min}$ (SD=3) and alcoholics had a mean of 28.7 $\mu\text{mol}/100 \text{ g/min}$ (SD=3) ($t=2.3$, $df=20$, $p < 0.05$). For the CTI study, normal subjects had a mean of 37.6 $\mu\text{mol}/100 \text{ g/min}$ (SD=3) and alcoholics had a mean of 31.2 $\mu\text{mol}/100 \text{ g/min}$ (SD=4) ($t=3.88$, $df=20$, $p < 0.001$). The difference in brain metabolic activity between the groups remained after correcting for age ($t=-3.63$, $df=10$, $p < 0.005$). Differences in regional absolute metabolic values between nor-

TABLE 2. Regional Metabolic Values ($\mu\text{mol}/100 \text{ g}/\text{min}$) for 22 Normal Subjects and 22 Alcoholics Studied With PET VI and CTI

Area	PET VI Study				CTI Study			
	Normal Subjects (N=11)		Alcoholics (N=11)		Normal Subjects (N=11)		Alcoholics (N=11)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Cortices								
Right frontal	36.1	4	31.2 ^a	4	55.0	6	41.9 ^b	4
Left frontal	33.0	4	28.2 ^c	5	55.6	7	41.3 ^b	4
Right parietal	34.4	4	29.9 ^c	4	50.5	4	39.6 ^b	4
Left parietal	34.6	4	28.5 ^b	4	51.3	6	39.7 ^b	4
Right temporal	36.2	4	32.4 ^c	4	50.3	5	40.0 ^b	3
Left temporal	35.3	4	31.6 ^c	4	49.9	6	39.8 ^b	3
Occipital	48.8	6	43.0 ^c	5	55.2	7	44.8 ^a	6
Basal ganglia	42.2	5	39.1	3	54.0	7	43.9 ^a	5
Thalamus	41.3	5	37.3	4	51.2	6	40.7 ^b	4
Cerebellum	31.8	4	28.7	3	43.9	4	38.1 ^a	4

^a $t > 3.2$, $p \leq 0.01$.^b $t > 4.5$, $p \leq 0.001$.^c $t > 2.21$, $p \leq 0.05$.

mal subjects and alcoholics ranged from 7% to 17% for the PET VI and from 14% to 25% for the CTI and were significant across most brain regions (table 2). The lower metabolic values obtained with the PET VI compared with the CTI are consistent with the lower spatial resolution of the former tomograph (30) and with the smaller volume of the regions of interest used to analyze the images from the CTI (figures 1 and 2).

Analyses of the normalized metabolic rates ("relative" measures) revealed that in the alcoholics certain brain regions were consistently lower than average. Figure 5 shows the average "relative" values for different brain regions in normal control subjects and in alcoholics for the PET VI and the CTI. Studies on both tomographs showed that the right frontal and left parietal cortices of alcoholics had disproportionately lower glucose metabolic rates than other parts of the brain. In the PET VI study, for the right frontal cortex, normal subjects had a mean of 1.11 (SD=0.04) and alcoholics had a mean of 1.05 (SD=0.06) ($t=2.51$, $df=20$, $p<0.02$) and for the left parietal cortex, normal subjects had a mean of 1.09 (SD=0.05) and alcoholics had a mean of 0.98 (SD=0.07) ($t=3.52$, $df=20$, $p<0.002$). In the CTI study, for the right frontal cortex, normal subjects had a mean of 1.46 (SD=0.05) and alcoholics had a mean of 1.35 (SD=0.10) ($t=3.02$, $df=20$, $p<0.01$) and for the left parietal cortex, normal subjects had a mean of 1.37 (SD=0.06) and alcoholics had a mean of 1.28 (SD=0.06) ($t=3.24$, $df=20$, $p<0.005$).

The correlation analyses showed a significant correlation between whole brain metabolism and number of days since last alcohol use. In the PET VI study, $r=0.63$, $df=10$, $p<0.05$, and in the CTI study, $r=0.83$, $df=10$, $p<0.01$ (figure 6). In contrast, the "relative" values for the right frontal and left parietal cortices were not correlated with the number of days since last alcohol use (PET VI right frontal cortex, $r=0.32$, $df=10$, n.s.; PET VI left parietal cortex, $r=0.20$, $df=10$, n.s.; CTI right frontal cortex, $r=0.27$, $df=10$, n.s.; CTI left parietal cortex, $r=0.37$, $df=10$, n.s.).

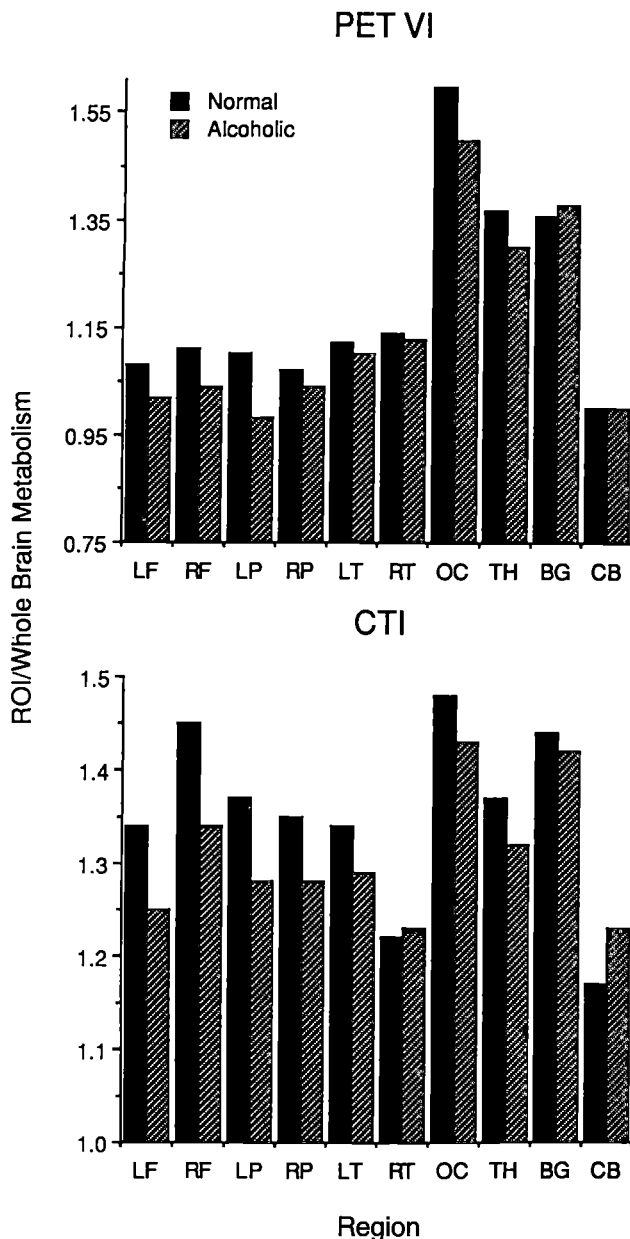
DISCUSSION

This study documents decreased brain glucose metabolism in neurologically intact otherwise healthy alcoholics. The decrease in whole brain metabolism related to the number of days since last alcohol use, suggesting that it represents, in part, a cerebral response to alcohol discontinuation. It is interesting to note that the brain metabolic changes associated with alcohol discontinuation occurred in the absence of signs and/or symptoms of alcohol withdrawal, suggesting that the cerebral response to alcohol withdrawal extends beyond the time period when the symptoms of withdrawal occur. The effects of alcohol withdrawal on brain function have been documented in both animals and humans (1) and could account for some of the brain structural recovery seen in alcoholics after 1 month of abstinence (8–10) as well as the increases in CBF seen in alcoholics after protracted abstinence (16). Brain metabolic changes during withdrawal could represent fluid and electrolyte changes (31), neurotransmitter adaptation (32, 33), and/or remyelination and neuronal plasticity (34). Evaluation of the degree of brain metabolic recovery in alcoholics after protracted withdrawal requires a prospective longitudinal study.

The decreases in whole brain metabolism are in agreement with previous studies showing consistent reductions in CBF in alcoholics (15, 18, 35). However, unlike the previous studies, in which the reductions in CBF were found to be related to neurological impairment and brain atrophy, this study demonstrates cerebral metabolic deficit in alcoholics with no neurological symptoms and with minimal or no brain morphological changes.

In addition, this investigation shows relative decreases in metabolism in the left parietal and right frontal cortices of alcoholics, with the parietal cortex showing the greatest decrease in metabolism. These regional findings are independent of the amount of time since last alcohol use and are identical to those reported in a

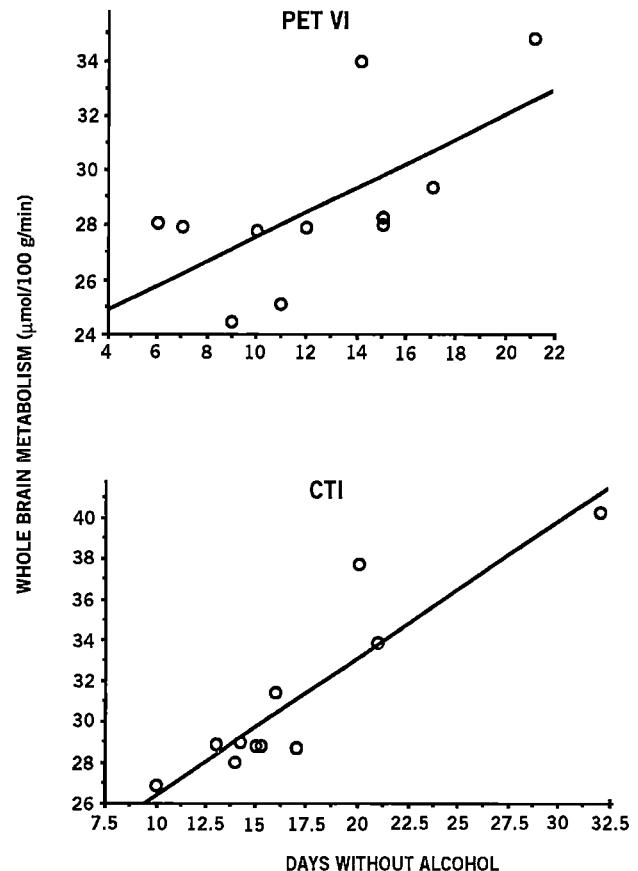
FIGURE 5. Relative Metabolic Values for Different Brain Regions in Normal Subjects and Alcoholics Studied With PET VI and CTI^a



^aROI=region of interest, LF=left frontal, RF=right frontal, LP=left parietal, RP=right parietal, LT=left temporal, RT=right temporal, OC=occipital, TH=thalamus, BG=basal ganglia, CB=cerebellum. Both studies showed that the left parietal and the right frontal cortices were the most affected regions in the alcoholics.

previous study done in a group of neurologically impaired alcoholics (20), suggesting that they result from the direct effects of alcohol on brain tissue rather than from alcohol-induced medical complications. Although the localization of the anatomical and/or functional deficits in the brain of alcoholics differs among investigators, the parietal and frontal cortices are consistently reported as being affected to a greater degree than other brain structures (1). This study reports regional later-

FIGURE 6. Correlation Between Number of Days Since Last Alcohol Use and Whole Brain Metabolism in Normal Subjects and Alcoholics Studied With PET VI and CTI



alization for the metabolic deficits in alcoholics (the right frontal cortex was more impaired than the left and the left parietal cortex more than the right), but it does not support the contention that the right hemisphere is more vulnerable to the toxic effects of alcohol than the left (1). Even though we excluded patients with evidence of moderate to severe cortical atrophy, more alcoholics than normal subjects showed evidence of mild degrees of morphological brain changes. The extent to which these structural changes contribute and/or reflect the dysfunction leading to decreased brain metabolism cannot be inferred from this investigation. Nor can this study rule out the possibility that the brain metabolic changes reported in these alcoholics antedated their use of alcohol.

This study shows that decreased brain metabolism in alcoholics is in part related to alcohol withdrawal and that brain metabolic dysfunction in alcoholics is not limited to neurologically affected patients.

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Are There Clinical Differences Between Familial and Nonfamilial Alzheimer's Disease?

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Objective: The purpose of the study was to determine whether there are differences in clinical characteristics in two groups of patients with Alzheimer's disease, those reported to have a family history of dementia and those without a family history of dementia. **Method:** Using a data set from an Alzheimer's disease patient registry, funded as part of a National Institute on Aging cooperative agreement, the authors made comparisons of sociodemographic and clinical variables in a group of 462 patients with Alzheimer's disease, 172 reported to have at least one first-degree relative with dementia and 290 classified with no family history. **Results:** Patients with a presumptive family history differed from those without a family history in two ways: the course of dementia was described as having a fast rather than a slow progression from onset of symptoms to diagnosis, and caregivers reported a higher prevalence of family history of psychiatric disorders. There were no significant differences in age at onset, duration, female gender, aphasia and apraxia, handedness, family history of Down's syndrome, or number of children, brothers, and sisters. **Conclusions:** The association of faster course and family history of psychiatric disorders in the patients with a family history of dementia is consistent with the hypothesis of heterogeneity, but the overall results could also be explained by a genetic-environmental model of Alzheimer's disease.

(Am J Psychiatry 1992; 149:1023-1027)

Since the possible role of heredity in the etiology of Alzheimer's disease was proposed by Flügel (1), there has been growing evidence for genetic contributions to the etiology of the disease. A higher prevalence of dementia among first-degree relatives of patients has been reported in most but not all population and case-control studies (2, 3). Numerous families with multiple members afflicted with Alzheimer's disease have been studied, and although an autosomal dominant form of Alzheimer's disease is supported by most of these family studies, others suggest polygenetic/multifactorial inheritance (2, 4). There is also evidence for genetic heterogeneity in familial Alzheimer's disease, with genes

on chromosome 21 implicated in early-onset and genes on chromosome 19 implicated in late-onset forms of the disease (5, 6).

The age-dependent onset of Alzheimer's disease has led to the suggestion that most cases of the disease are familial, with the argument that many cases of familial Alzheimer's disease are incorrectly classified as nonfamilial or sporadic because older relatives of probands either are not evaluated adequately or die before growing old enough to be at risk (7, 8). However, several investigators have argued that the occurrence of familial Alzheimer's disease does not negate the role of environmental causes in some or most cases of Alzheimer's disease (2, 9). Head injury, infectious agents, environmental toxins, and advanced maternal age have all been implicated as factors linked to Alzheimer's disease (2, 9-15).

A few investigators have looked for clinical differences in patients with familial and sporadic Alzheimer's disease to test the hypothesis of heterogeneity in the etiology of the disease; that is, clinical features of familial Alzheimer's disease would distinguish it from nonfamilial Alzheimer's disease if they represent two different diseases. However, results have been inconsistent.

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Breitner and Folstein (16) found that relatives of Alzheimer's disease probands with aphasia, apraxia, or agraphia had a 50% risk of developing Alzheimer's disease, while relatives of probands without such symptoms did not have a high risk. Mohs et al. (17) observed that the morbid risk of Alzheimer's disease in first-degree relatives of patients was 46% by 86 years of age. Although this series of Alzheimer's disease probands was not selected for aphasia and apraxia, only 6% did not have these symptoms. Knesevich et al. (18), as well as Edwards et al. (19), have not replicated the predictive value of aphasia.

At least two groups have reported that patients with familial Alzheimer's disease had an earlier age at onset than patients with the nonfamilial form of the disease; however, others have not replicated the simple association between familial Alzheimer's disease and age at onset (19–21). Results of several studies indicate that there are early-onset and late-onset forms of familial Alzheimer's disease and that age at onset is specific for different families (2, 7, 22–24).

The availability of a large pool of dementia patients in an Alzheimer's disease patient registry provided a research opportunity to select patients with Alzheimer's disease in order to analyze clinical differences between familial and nonfamilial forms of the disease. The objectives were to determine if earlier age at onset, faster course, aphasia, apraxia, female gender, history of Down's syndrome, and other reported factors differentiated the two groups and to test for other clinical differences in patients.

METHOD

Subjects

The subjects for this analysis were patients with Alzheimer's disease selected from an Alzheimer's disease patient registry known as the Prototype Alzheimer's Collaborative Team. The Prototype Alzheimer's Collaborative Team was established to study the feasibility and costs of establishing and operating a multisite registry for research on Alzheimer's disease and other dementias. Methods and procedures for case ascertainment, case enrollment, and data management, as well as a sociodemographic profile of the registry population, have been described (25).

Briefly, the Prototype Alzheimer's Collaborative Team consists of a Data Coordinating and Analysis Center at the University of Illinois at Chicago that registered patients diagnosed at six medical sites. Four were specialized Alzheimer's disease clinical programs: the Memory Disorders Clinic, Mount Sinai Hospital and Medical Center, Miami Beach; the Memory Disorders Clinic, the University of Miami, Jackson Memorial Hospital; the Regional Alzheimer's Disease Center, Southern Illinois University School of Medicine, Springfield; and the Alzheimer's Disease Center, Michael Reese Hospital and Medical Center, Chicago. Two were specialized

geriatric clinical programs: the Geriatric Clinic at the University of Chicago School of Medicine and the Geriatrics Institute, University of Wisconsin-Milwaukee Clinical Campus.

The Prototype Alzheimer's Collaborative Team contains diagnostic, psychosocial, and sociodemographic information on a total of 1,402 patients with Alzheimer's disease and related dementias diagnosed between 1987 and 1989. Enrolled patients were 40 years and older and living in the community at the time of diagnosis. The minimum enrollment criterion was a clinical diagnosis of dementia with documentation from physical, psychiatric, neurological, and psychological examinations. A total of 671 patients met diagnostic criteria for Alzheimer's disease. Most were diagnosed according to *DSM-III-R* or the criteria of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (26), and 90% of patients were diagnosed with both criteria. A few patients were diagnosed according to *DSM-III*.

We analyzed clinical characteristics of those 462 Prototype Alzheimer's Collaborative Team patients who met the criteria for probable Alzheimer's disease of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association, *DSM-III-R* criteria for Alzheimer's disease, or *DSM-III* criteria for primary degenerative dementia and who also were reported to have either a family history or no family history of dementia. A total of 172 patients with at least one first-degree relative (i.e., parent, child, or sibling) with dementia were classified as having a family history. The remaining 290 patients with no family history were classified as suspected of having no family history. Patients with Alzheimer's disease with a family history in only second-degree relatives ($N=27$) or with an unknown family history ($N=182$) were excluded from the analysis.

The case enrollment form contained data on family history of dementia, other psychiatric disorders, other neurological disorders, and Down's syndrome. The specific questions on family history of dementia were, "Is there a family history of dementia?" and "Specify the relationship to patient." Data coded reflected results of clinical interviews with primary caregivers, 90% of whom were spouses or first-degree relatives and 10% of whom were in-laws or other relatives.

Clinical Variables

The following groups of variables from the Prototype Alzheimer's Collaborative Team case enrollment form were used in this analysis: sociodemographic information; clinical diagnostic data, including the results of the medical, psychiatric, and neurological examinations; ratings of functional impairment and mental status at diagnosis; and results of patient CT scans and magnetic resonance imaging (MRI) at diagnosis. The format for recording specific clinical diagnostic data on the case

TABLE 1. Characteristics of 462 Patients With Probable Alzheimer's Disease With or Without a Family History of Dementia

Item	Family History (N=172)				No Family History (N=290)			
	Mean	SD	N	%	Mean	SD	N	%
Age (years)	74.0	6.9			74.9	8.4		
Men			72	41.9			90	31.0
Women			100	58.1			200	69.0
Education (years)	12.0	3.4			11.4	3.6		
Mini-Mental State score	16.0	7.4			15.0	7.5		

enrollment form was as follows: 1) seven items describing patient behaviors that precipitated the diagnostic workup, 2) a 16-item checklist of psychiatric symptoms, 3) a 26-item checklist of medical conditions, 4) a 24-item checklist of neurological symptoms, 5) a six-item checklist of impairments in activities of daily living, 6) an eight-item checklist describing findings from CT and MRI, and 7) the Mini-Mental State examination score (27).

Data Analysis

Data were analyzed comparing demographic variables in the groups with family histories and no family histories of dementia, as well as several clinical characteristics previously reported to be associated with familial Alzheimer's disease, including age at onset, duration, rapidity of progression, handedness, female gender, and the presence of aphasia or apraxia. We also examined conditions reported to occur with higher frequency in the families of individuals with Alzheimer's disease, including Down's syndrome (28) and psychiatric disorders (29). Furthermore, because of suggestions that familial forms of dementia such as Huntington's chorea might be associated with higher rates of fertility (30), we compared the number of children of patients with Alzheimer's disease in each group.

Parametric variables were analyzed with the Student's *t* test between groups with no family histories and family histories. For categorical data a 2x2 Yates's-corrected chi-square with one degree of freedom was used, except when cells were less than five, in which case a Fisher's exact probability test was calculated. A Bonferroni correction (31) was used to adjust for the multiple comparisons of patient variables.

RESULTS

Demographic characteristics of the groups with or without presumptive family histories of dementia are shown in table 1. There were no significant differences in age, gender, education, or severity of cognitive impairment according to the Mini-Mental State score. Table 2 presents the results of analyses of factors previously reported to be associated with familial Alzheimer's

TABLE 2. Clinical Factors Associated With Familial Alzheimer's Disease in 462 Patients With Probable Alzheimer's Disease With or Without a Family History of Dementia

Factor	Family History (N=172)				No Family History (N=290)			
	Mean	SD	N	%	Mean	SD	N	%
Dementia								
Age at onset (years)	69.8	7.9			71.4	8.8		
Duration (years)	4.1	3.1			3.3	2.6		
Increasing progression ^a			132	76.7			163	56.2
Aphasia			41	23.8			96	33.1
Apraxia			53	30.8			76	26.2
Right-handedness			168	97.7			273	94.1
Family history								
Down's syndrome			13	7.6			6	2.1
Psychiatric illness ^b			32	18.6			21	7.2
Number of children	2.6	2.0			2.4	1.8		
Number of brothers	2.2	2.0			2.1	1.9		
Number of sisters	2.0	1.6			1.9	1.6		

^a $\chi^2=12.8$, *df*=1, *p*=0.004.

^b $\chi^2=15.8$, *df*=1, *p*=0.0009.

mer's disease. Two significant differences emerged. An increasing rate of decline, in contrast to a gradual change from onset of symptoms to diagnosis, occurred more frequently in the group with a family history of dementia than in the group with no family history (76.7% versus 56.2%, *p*=0.004). Family history of psychiatric disorders was more prevalent in the group with a family history than in the group with no family history (18.6% versus 7.2%, *p*=0.0009). There were no significant differences in age at onset, duration, female gender, aphasia, apraxia, handedness, family history of Down's syndrome, or number of children, brothers and sisters. No significant differences emerged for any of the remaining clinical diagnostic variables.

DISCUSSION

Only a few clinical characteristics differentiated patient groups with presumptive familial and nonfamilial Alzheimer's disease. Early age at onset, duration, female gender, the presence of aphasia or apraxia, handedness, family history of Down's syndrome, and the number of children, brothers, and sisters did not distinguish the two groups of patients with Alzheimer's disease. Our results are consistent with the recent findings of Edwards et al. (19), who studied 151 index patients, 84 of whom had at least one relative with dementia. The lack of differences in both of these studies suggests that there is a similar clinical presentation in familial and nonfamilial Alzheimer's disease.

The major limitation of this study affecting the interpretation of our results is the possibility of classification errors in the accuracy of the diagnosis of Alzheimer's disease registry patients and the family history groupings. Since classification errors favor the null hypothesis unless a systematic bias is operating, misclassifications

increase the probability of not finding significant differences (19).

The diagnosis of Alzheimer's disease and related dementias in the Prototype Alzheimer's Collaborative Team registry was made by clinical staff at six clinical sites participating in a study of case ascertainment, case enrollment, and data management problems associated with developing and implementing a large-scale, multisite dementia registry. To reduce the impact of variability among clinicians, we restricted our analysis group to individuals who met *DSM-III-R* criteria for Alzheimer's disease, National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association criteria for probable Alzheimer's disease, and *DSM-III* criteria for primary degenerative dementia.

We classified patient groups by the available history of first-degree relatives who had dementia, and both the underreporting of dementia and the reporting of dementias other than Alzheimer's disease could cause classification errors. Although Alzheimer's disease is the most common cause of dementia, it is likely that some of the individuals with a family history described in this study had first-degree relatives with dementia that was not Alzheimer's disease.

The more rapid rate of change from onset of dementia symptoms to diagnosis, which distinguished the group with a family history, refers to an average period of 4.1 years in the group with a family history and 3.3 years in the group with no family history. This difference was only marginally significant with the Bonferroni correction ($F=7.10$, $df=1, 460$, $p=0.007$). Our results are consistent with the more rapid progression to death in familial Alzheimer's disease reported by Heston et al. (28). However, evaluating an increasing rate of decline may be a difficult clinical judgment, especially in the absence of specific criteria. It might also be confounded by a clinician's knowledge of the patient's family history and frequency of patient visits.

The higher frequency of psychiatric illness in familial Alzheimer's disease is consistent with the work of Martin et al. (29), who are the only others we know who have reported a greater occurrence of psychiatric illness in relatives of patients with Alzheimer's disease. However, they did not distinguish between patients with Alzheimer's disease with or without family histories of dementia. It is possible that there was a response bias in Prototype Alzheimer's Collaborative Team patients in which more family information might have been available for probands with a family history than for probands with no family history, leading to the documentation of other disorders at a higher rate.

Although the average age at onset was not significantly different between our two patient groups, this result might be expected if age at onset is specific for different families. Intensive study of our Prototype Alzheimer's Collaborative Team probands with standardized pedigrees and validation of Alzheimer's disease in first-degree relatives may be needed to rigorously test for clinical differences and the hypothesis of hetero-

geneity. Our findings of a more rapid course and a family history of psychiatric problems in familial Alzheimer's disease are not inconsistent with the hypothesis of heterogeneity and deserve further study.

In summary, our patients with family histories and no family histories of Alzheimer's disease appear to be largely clinically indistinguishable, not unlike other neuropsychiatric disorders, e.g., Charcot-Marie-Tooth disease, olivopontocerebellar ataxia, torsion distress, and schizophrenia (2). One explanation for these findings could be a genetic-environmental model of Alzheimer's disease that does not require clinical differences between patients with a family history and those with no family history, but only etiological differences (19). Thus, genetic factors, environmental exposures, or a combination could trigger the onset of Alzheimer's disease and its clinical symptoms.

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Bright Light Treatment of Behavioral and Sleep Disturbances in Patients With Alzheimer's Disease

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Objective: The authors tested the hypothesis that evening bright light pulses would improve sleep-wake patterns and reduce agitation in patients with Alzheimer's disease who have severe sundowning (a syndrome of recurring confusion and increased agitation in the late afternoon or early evening) and sleep disorders. **Method:** Ten inpatients with Alzheimer's disease on a research ward of a veterans' hospital were studied in an open clinical trial. All patients had sundowning behavior and sleep disturbances. After a week of baseline measurements, patients received 2 hours/day of exposure to bright light between 7:00 p.m. and 9:00 p.m. for 1 week. During the baseline week, the treatment week, and a posttreatment week, patients were rated by nurses for agitation, sleep-wake patterns, use of restraints, and use of prescribed-as-needed medication. On the last 2 days of each week, patients wore activity monitors. Activity counts were analyzed for circadian rhythmicity. **Results:** Clinical ratings of sleep-wakefulness on the evening nursing shift improved with light treatment in eight of the 10 patients. The proportion of total daily activity occurring during the nighttime decreased during the light-treatment week. The relative amplitude of the circadian locomotor activity rhythm, a measure of its stability, increased during the light-treatment week. More severe sundowning at baseline predicted greater clinical improvement. **Conclusions:** Evening bright light pulses may ameliorate sleep-wake cycle disturbances in some patients with Alzheimer's disease. This effect may be mediated through a chronobiological mechanism.

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Behavioral disorders in patients with Alzheimer's disease markedly increase the burden of their caregivers. Sleep disturbances in particular and agitation, restlessness, and pacing more generally often cause caregiver stress and burnout and may precipitate institutionalization of the patient (1). "Sundowning," a syndrome of recurring confusion and increased agitation in the late afternoon or early evening, is common among patients with Alzheimer's disease in nursing homes (2). Neuroleptic medications are frequently prescribed for behavioral disorders in demented patients, but the

available evidence suggests that they are more effective than placebo alone in only 18 of 100 treated patients (3). In addition, neuroleptic use in demented patients is commonly associated with side effects that may lead to worsening of behavior and even of cognition (1, 4).

Fragmented sleep-wake cycles and sundowning are characterized by inappropriately timed rest and activity, suggesting that these syndromes may be mediated by abnormalities of the circadian timekeeping system in Alzheimer's disease. The circadian locomotor activity rhythm was found to have a lower amplitude and delayed acrophase (the time of peak daily activity) in patients with Alzheimer's disease than in healthy elderly control subjects in one study (5). The hypothesis of a disordered circadian pacemaker in some patients with Alzheimer's disease is supported by chronobiological studies of sleep and endocrine measures (6, 7) and by neuropathological studies reporting cell loss in the suprachiasmatic nucleus of the hypothalamus (8). However, the circadian rhythm of core body temperature may remain intact in Alzheimer's disease, suggesting that manipulation of the circadian system may still be possible even in demented individuals (9).

Investigators have found that properly timed bright

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light exposure may induce phase shifts of the circadian pacemaker and may augment the amplitude of the circadian rhythm (10). An association between light exposure and behavioral disorders in Alzheimer's disease is suggested by the finding that patients with Alzheimer's disease living at home were exposed to significantly less bright light than healthy control subjects (11) and by a report of an apparent increase in sundowning behavior in nursing home patients during the winter months (12). Bright light treatment improved the sleep efficiency of normal elderly subjects with sleep maintenance disturbance in a recent study (13), and some demented patients with sleep-wake disturbances improved with phototherapy in two other studies (14, 15).

The present study sought to test the hypothesis that bright light pulses would reduce agitation and improve the sleep patterns of patients with Alzheimer's disease.

METHOD

Ten inpatients (nine men, one woman; mean age=70.1 years, SD=5.1) on the dementia study unit of a veterans' hospital were studied for 3 weeks. All met *DSM-III-R* criteria for primary degenerative dementia and National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association criteria for Alzheimer's disease (16) (mean age of onset=60.4 years, SD=8.1), and all were moderately to severely demented. The mean duration of their illness was 9.3 years (SD=6.7), their mean Mini-Mental State Examination (17) score was 0.6 (SD=1.1), and their mean Activities of Daily Living (18) score was 5.3 (SD=0.8) (the range of scores on this scale is 0–6, and higher scores indicate more impairment). Patients were identified by nursing staff as sundowners according to the following definition of this syndrome: the recurrent appearance or exacerbation of behavioral disturbances such as agitation, pacing, restlessness, yelling, or shouting in the afternoon or evening. Most of the patients began pacing or yelling between 2:00 p.m. and 4:00 p.m. Patients also exhibited sleep disturbances characterized by frequent daytime napping and nighttime awakenings. None of the patients had any substantial intercurrent medical illnesses, and none had substantial cataracts. Eight of the 10 patients were taking standing doses of neuroleptic medication, one was taking regular doses of diphenhydramine, and one was not taking any regular psychotropic medication. All 10 had prescriptions for as-needed neuroleptic or benzodiazepine medication. Written informed consent was obtained from relatives in accordance with standard hospital practice.

Nurses performed daily ratings each shift (day, evening, and night) for agitation and sleep-wakefulness disturbances on a 0–3 scale (0=none or minimal, 1=mild, 2=moderate, 3=severe). Higher scores for sleep-wake cycle disturbances represented more time awake during the night or more time asleep during the day or

evening. Scores for each shift represented ratings for the entire 8-hour period. The use of restraints (0=none, 1=one physical restraint such as a posey, geri-chair, bed rails, or hand mitts; 2=two or more forms of physical restraint) and of prescribed-as-needed medication (0=none, 1=one administration, 2=two or more administrations) were recorded for each shift. Locomotor activity was recorded for 48 hours at the conclusion of each study week by using a portable piezoelectric activity monitor with solid-state memory. The monitor was placed in the pocket of a vest worn over the patient's clothing and positioned at waist level.

During each evening of week 2 between 7:00 and 9:00 p.m., patients received 2 hours of exposure to approximately 1500–2000 lux while seated in a geri-chair facing the light box and restrained by a tray. The light box consisted of three U-shaped fluorescent bulbs (Phillips FB40/CW). Medication changes were not permitted during the 3 weeks of the study.

Nonparametric tests (Friedman's analysis of variance and Wilcoxon matched-pairs test) were used to compare weekly summed ratings of individual clinical measures over the 3 weeks of the study (baseline, treatment, and posttreatment). Relationships between baseline predictors of response and treatment effects were analyzed by using Pearson correlation coefficients. Locomotor activity data were analyzed for percent of activity for each daily shift. A cosinor analysis (19) was used to calculate the following circadian rhythm measures in the raw activity data: mesor (mean daily activity level), amplitude, acrophase, and period. Relative amplitude was calculated as the ratio of the circadian amplitude to the mesor in order to correct for differences in magnitude of the activity counts. Interdaily stability and intradaily variability also were calculated, as described by Witting et al. (20).

RESULTS

Clinical ratings of sleep-wakefulness on the evening shift improved with light treatment in eight of the 10 patients. The mean score of all 10 patients declined from 6.2 at baseline to 3.0 during the treatment week and further declined to 2.3 during the posttreatment week ($\chi^2=7.35$; $df=2$; $p=0.03$, Friedman analysis of variance [ANOVA]; for week 1 versus week 2, $z=-2.04$, $p=0.04$; for week 1 versus week 3, $z=-2.31$, $p=0.02$, Wilcoxon matched-pairs signed-ranks test). This finding was supported by some of the objective measures obtained from the activity monitor data (tables 1 and 2). Intradaily variability of the activity monitor counts (a measurement of the combined severity of daytime napping and nighttime wakefulness) decreased during week 2 in nine of the patients, although it returned to baseline at week 3 (mean for week 1=1.04; mean for week 2=0.71; mean for week 3=1.06; $F=3.87$, $df=2, 26$, $p=0.03$). Interdaily stability did not change. Percent of nocturnal activity (the proportion of total daily activity counts occurring from 11:00 p.m. through 7:00 a.m.) decreased from baseline to the light-

TABLE 1. Group Activity Data for 10 Patients With Alzheimer's Disease Before (Week 1), During (Week 2), and After (Week 3) Light Treatment

Week	Nocturnal Activity (%)		Interdaily Stability ^a		Intradaily Variability ^b		Mesor ^c		Relative Amplitude		Acrophase (time) ^d	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
1	18.4	7.9	0.68	0.17	1.04	0.34	393	192	0.65	0.36	16:15	120
2	11.6	6.6	0.71	0.12	0.71	0.22	401	222	0.90	0.23	15:23	108
3	17.1	11.2	0.63	0.09	1.06	0.38	400	231	0.69	0.41	15:21	129

^aA measure of the day-to-day variability in the cycle of activity counts; a higher value indicates less variability.

^bA measure of the within-day variability of the activity counts; a higher value indicates more variability between successive 5-minute epochs and thus more transitions between rest (or sleep) and activity.

^cThe mean daily activity count.

^dThe calculated clock time of the peak of the locomotor activity daily cycle according to a 24-hour clock plus or minus minutes.

TABLE 2. Activity Data for Individual Patients With Alzheimer's Disease Before (Week 1) and During (Week 2) Light Treatment^a

Patient	Sleep-Wake Rating		Nocturnal Activity (%)		Intradaily Variability		Relative Amplitude		Number of Measures Improved
	Week 1	Week 2	Week 1	Week 2	Week 1	Week 2	Week 1	Week 2	
1	7	2	19.9	12.9	1.03	0.71	0.61	0.99	4
2	9	5	26.5	10.7	1.23	0.62	0.30	0.82	4
3	9	2	26.5	23.9	1.57	0.96	0.35	0.50	4
4	4	2	21.9	1.2	0.53	0.49	0.41	1.13	4
5	0	3	20.6	10.8	0.82	0.54	0.70	0.92	3
6	12	3	18.7	16.7	1.55	1.06	0.36	0.73	4
7	6	10	23.5	12.4	1.10	0.42	0.52	0.97	3
8	6	1	1.6	1.5	0.71	0.58	1.35	1.24	3
9	1	0	8.1	12.7	0.90	0.93	1.21	1.08	1
10	8	2	17.1	13.1	0.93	0.73	0.70	0.61	3

^aImprovement is indicated by an increase in the relative amplitude and by a decrease in all other measures.

treatment week in nine patients (mean for week 1=18.4% versus mean for week 2=11.6%; $t=2.84$, $df=9$, $p=0.02$) and also increased during week 3 (mean=17.1%), although this change was not statistically significant. According to the results of the cosinor analysis, cosinor fits were statistically significant for all patients during each study week. The relative amplitude of the rest-activity circadian rhythm increased from baseline to the light-treatment week in seven patients (mean for week 1=0.65 versus mean for week 2=0.90; $t=2.69$, $df=9$, $p=0.02$). The mesor and the period did not change. The locomotor activity acrophase shifted earlier by about an hour from baseline to weeks 2 and 3 (4:15 p.m. to 3:23 p.m. to 3:21 p.m.), but this change was not statistically significant.

Clinical ratings of agitation, use of restraints, and use of as-needed medication did not change on any shift. Three patients received two or fewer doses of prescribed-as-needed medication during the 3 weeks of the study; the remaining seven patients received from 7 to 15 doses of such medication. In eight patients, weekly total use of prescribed-as-needed medication for each individual did not vary by more than two doses for any shift. In one patient (patient 5), use of prescribed-as-needed medication during the daytime shift increased from one dose at baseline to five doses during the treatment week; this patient's daytime agitation score increased from 8 to 11, and his mean daytime activity counts did not change (7,298 versus 7,534), suggesting that the increased use of prescribed-as-needed medication was not associated with clinical improvement or a

decrease in activity. In patient 6, six doses of prescribed-as-needed medication were used during the evening shift during the baseline and treatment weeks, but none were used during week 3. This patient had the largest improvement in sleep-wakefulness by nurse ratings during the treatment week and a further improvement in week 3, suggesting that use of prescribed-as-needed medication declined in response to the observed improvement. Overall, these data suggest that use of prescribed-as-needed medication did not have a direct effect on the rest-activity data or on the observed clinical benefits of light treatment.

When the clinical ratings for the last two days of each week were examined separately, the mean rank scores for sleep-wakefulness on the evening shift were nearly identical to those obtained by using the whole week summation. Results of ANOVA using these ratings was not statistically significant due to the much smaller number of data points. Other clinical ratings for the last 2 days of each week also did not change significantly.

A composite baseline score for the severity of sundowning was calculated by subtracting the summed week 1 daytime shift scores on all four clinical measures from the summed week 1 evening shift scores. One patient had a neutral sundowning score (i.e., equal to 0); the scores of the other patients ranged from 3 to 20, indicating that behaviors were in fact worse in the evening (mean sundowning score=10.9, $SD=7.0$). The severity of sundowning at baseline correlated with lower relative amplitudes of the rest-activity circadian cycle calculated from the ac-

tivity monitor data ($r=0.74$, $df=8$, $p=0.02$). Sundowning scores calculated similarly for week 2 (mean=9.2, $SD=8.0$) and week 3 (mean=3.4, $SD=3.7$) revealed a significant decrease for the posttreatment week ($\chi^2=6.2$, $df=2$, $p<0.05$, Friedman ANOVA).

A composite improvement score was calculated by subtracting the summed evening shift ratings on all clinical measures during week 2 from those of week 1. A persistence-of-effect measure was calculated by a similar subtraction of week 3 scores from week 1 scores. There was a positive correlation between the severity of sundowning at baseline and the degree of improvement with light treatment during the treatment week ($r=0.65$, $df=8$, $p=0.02$) and during the posttreatment week ($r=0.77$, $df=8$, $p=0.004$) (figure 1).

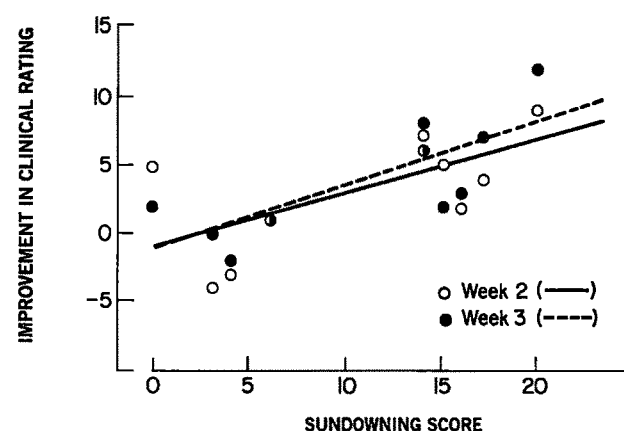
DISCUSSION

Evening bright light pulses administered for a week to patients with Alzheimer's disease who had sundowning behavior and sleep-wake cycle disturbances were associated with nurse ratings of improved sleep-wake behavior during the evening and with a decline in a measure of the severity of sundowning during the posttreatment week. Sleep-wake patterns (intradaily variability) also improved, and nighttime activity decreased, according to activity monitor measurements. These results suggest that bright light treatment may ameliorate sleep-wake cycle disturbances in some patients with Alzheimer's disease. Two reports from a group in Japan (14, 15) also suggest that phototherapy may be effective in patients with dementia, although patients with multi-infarct dementia were more likely to respond than those with Alzheimer's disease, and morning light was more effective than evening light.

This pilot study used an open-treatment, uncontrolled design. Nurses were aware of the treatment and its postulated effect, which could have influenced ratings. However, improvements in sleep-wake measures in week 2 persisted into week 3, and the sundowning score declined only in week 3, suggesting that nurse ratings were not influenced by the presence of the light treatment itself. In addition, the nurses' clinical ratings were partially corroborated by the data from the activity monitor. Nevertheless, the results of this study indicate a need for further study of bright light treatment in Alzheimer's disease using blinded raters and a no-treatment (or sham-treatment) control group.

Corresponding improvements were found according to clinical ratings and activity monitor data during week 2, but although clinical ratings suggested persistence of improvement into the posttreatment week, the activity monitor measures generally returned to baseline during the posttreatment week. It may be that these two methods of assessment are sensitive to somewhat different effects. Further studies should use both methods, perhaps with more specific, detailed, and frequent clinical ratings to help define the relationship between clinical behaviors and the circadian cycle of rest-activ-

FIGURE 1. Relation Between Severity of Sundowning and Response to Light Treatment in 10 Patients With Alzheimer's Disease



ity. Longer-term studies will be needed to determine whether beneficial effects persist over time, to document the time course of a return to baseline after treatment discontinuation, and to correlate these results with chronobiological changes. Such studies may shed light on the mechanism of action of phototherapy on sleep and behavior.

Future studies also should monitor activity for longer than 48 hours. In this study, cosinor fits were statistically significant for each of the patients during all study weeks, justifying the use of such an analysis for estimating the relative amplitude of the circadian locomotor cycle. However, the rest-activity cycle normally has a labile period (cycle duration), with cycle-to-cycle deviations that may be influenced by the environment and by conscious decisions (21). In addition, patients with Alzheimer's disease may have more day-to-day variability in their locomotor activity cycles than elderly patients without Alzheimer's disease (5, 20). On one measure of this day-to-day variability—interdaily stability—patients with Alzheimer's disease in this study had a mean value of 0.68. This finding is comparable to the 0.64 found in a previous study with similar patients, experimental conditions, and equipment (5) and is lower than the 0.81 found for age-matched control subjects in that study. In the current study, therefore, more cycles would have been required for analysis to determine true changes in locomotor period or phase, and no firm conclusions regarding these measures of the circadian locomotor cycle may be drawn from the data.

More severe sundowning at baseline predicted greater improvement on a composite of the clinical ratings. Sundowning also was associated with reduced amplitude of the circadian rest-activity cycle, and amplitude increased with light treatment. The amplitude of a circadian rhythm is thought to be the most direct reflection of the stability of that rhythm (22). Thus, these findings suggest that sundowning may be associated with disturbed circadian rhythms and that the severity of these disturbances may predict response to bright light.

Evening light pulses were used in this study because the behaviors we hoped to affect are most prominent later in the day. Studies of the phase-response curves for the effect of light pulses on circadian rhythms find phase-delays when light is given at the end of the subjective day and early in the subjective night (23). It is possible that evening light in this study exerted its effect by phase-delaying the circadian core body temperature cycle, restoring a more normal phase relationship between this cycle and a phase-delayed rest-activity rhythm. This hypothesis of a chronobiological mechanism is supported by the finding from another study that bright light pulses timed to produce an average phase-delay in core body temperature of about 2 hours were associated with significant improvements in sleep maintenance in older subjects (13). A postulated chronobiological mechanism for the effect of light on sleep would predict that treatment effects should lag behind light exposure, since steady-state phase shifts require many transient cycles to develop (23). Thus, such a mechanism is not supported by our failure to find more robust effects when the clinical data from the last 2 days of week 2 were examined separately but is supported by the persistence of treatment effects into the posttreatment week of the study. Another possible chronobiological explanation is that the beneficial behavioral effect is mediated through an increased amplitude of the endogenous circadian pacemaker, such as was observed for the locomotor activity rhythm.

Further studies should test the chronobiological hypotheses generated by this study by measuring the effect of bright light on temperature and other rhythms in behaviorally disturbed patients with Alzheimer's disease. Different baseline circadian rhythms may suggest the use of bright light pulses at other times of the day in some patients, possibly with greater effects when treatment is individualized in such a manner. Nevertheless, individual differences in response, or lack of response in some subjects, still may result from differences in sensitivity to light among patients with Alzheimer's disease, as suggested by the finding of axonal degeneration in the optic nerves of such patients (24).

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Hypothalamic-Pituitary-Adrenal Axis Hyperactivity and Psychosis: Recovery During an 8-Year Follow-Up

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***Objective:** An earlier study showed that the results of the dexamethasone suppression test (DST) predicted outcome among patients with a functional psychosis followed to 1 year. The present study was undertaken to replicate these findings with a different patient group and a longer follow-up. **Method:** Ninety-two inpatients with nonorganic, nonmanic psychoses had DSTs during their hospitalizations. Raters who were blind to DST results, and to baseline chart or research diagnoses, conducted personal interviews with 71 of the patients 8 years later. **Results:** Patients who had been nonsuppressors on the DST were five times more likely than those who had been suppressors to be free of psychotic features and to exhibit insight at the follow-up interview (42% versus 8%). Prognostic differences between these groups were clear within the first year of follow-up. Baseline diagnoses also strongly predicted outcome, even among DST nonsuppressors, and DST results had no prognostic significance among patients with a baseline diagnosis of schizophrenia. Later ages at onset and short episode durations at intake also predicted recovery, but baseline DST suppressor status remained important after control for these factors. **Conclusions:** The findings of this study and those of the earlier follow-up suggest that among patients with a functional psychosis, nonsuppression on the DST is prognostically important, particularly after the exclusion of those who meet narrow criteria for schizophrenia.*

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Three lines of evidence converge to suggest that hypothalamic-pituitary-adrenal (HPA) axis abnormalities have prognostic relevance to the functional psychoses. The first arises from the traditional view, supported by both short-term (1) and long-term (2) follow-up studies, that psychotic affective disorder has a much more favorable prognosis than does schizophrenia. The second consists of outcome and family studies which indicate that the diagnoses of schizoaffective disorder, schizophreniform disorder, and affective disorder with mood-incongruent psychotic features designate relatively heterogeneous groups composed both of patients with schizophrenia and of patients with affective disorder (3). The third line of evidence suggests that nonsuppression on the dexamethasone suppression test (DST) is common among patients with severe, endogenous, primary, or psychotic major depression but rare among patients with schizophrenia (4-8). Together, these trends indicate that among patients with a non-

manic, functional psychosis, those with nonsuppression on the DST will have better outcomes than those with normal DST results. Furthermore, this prediction should be more robust with greater diagnostic heterogeneity, i.e., among patients with schizoaffective disorder or major depressive disorder with mood-incongruent psychotic features.

This third assumption is much less secure than the first two; diagnostic specificity was much lower in other studies (9-12), but disparities between those two sets of studies have not been reconciled, nor are there obvious reasons for falsely high diagnostic specificity. In fact, a meta-analysis of 26 relevant studies (8) showed that overall, 19% of patients with schizophrenia but 67% of patients with psychotic major depression were DST nonsuppressors and that dexamethasone dose, timing of postdexamethasone cortisol sampling, and the presence of ongoing treatment did not account for the substantial differences in nonsuppression rates seen across studies. In addition, while the rate of nonsuppression among schizophrenic patients was much lower than that among patients with psychotic depression, it was significantly higher than that seen among normal control subjects (7%). The misclassification of psychotic major depression as schizophrenia undoubtedly accounts for some DST nonsuppression among schizo-

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phrenic patients and for some of the inconsistencies across studies, but only very high rates of misdiagnosis would explain differences of this magnitude. Instead, certain subtypes of schizophrenia, such as those with predominantly negative symptoms (13, 14), may predispose patients to DST nonsuppression, and this nonsuppression may reflect physiological processes different from those producing nonsuppression among patients with psychotic major depression. There is no consensus on the existence or the nature of this subgroup, however (15, 16).

Despite the occurrence of DST nonsuppression among patients with "true" schizophrenia, the much higher likelihood of nonsuppression among patients with psychotic depression may nevertheless render the test prognostically useful in diagnostically mixed groups. This is provided, of course, that the prognosis for schizophrenia is much worse than that for affective disorder, and a number of follow-up studies suggest that this is so (2, 17). Thus, if the likelihoods of nonsuppression are 17% and 67% for patients with schizophrenia and patients with psychotic affective disorder, respectively (8), if the prognosis of affective disorder is generally good and that of schizophrenia is generally bad, and if as many as one-third of patients who exhibit both psychotic and depressive symptoms prove, in time, to have outcomes that suggest schizophrenia (18), then, among patients who show such mixed features, nonsuppressors on the DST should be approximately twice as likely as suppressors to have good outcomes.

Only a few researchers have tested such predictions. Targum (19) studied 21 schizophreniform patients for 6 months and found a modest but nonsignificant association between baseline nonsuppression on the DST and recovery. However, Maj et al. (20) detected no globally rated difference between 13 initial suppressors and nonsuppressors after 3 years. Tandon et al. (21) studied 33 patients with *DSM-III-R* schizophrenia to 1 year and noted better outcomes for nonsuppressors at 4 weeks but not at 1 year. Finally, Coryell and Zimmerman (22) studied a diagnostically mixed group of psychotic patients for 1 year and found a robust relationship between baseline DST nonsuppression and outcome. Among psychotic patients who did not meet criteria for schizophrenia, those who were definite nonsuppressors at baseline were 2.7 times more likely than DST suppressors to be free of delusions and insightful 1 year later.

The reasoning described earlier, as well as the practical implications of our earlier findings (22), led us to attempt a replication with a different patient group studied over a longer period. In doing so we wished, first, to determine whether DST results had practical and reproducible prognostic significance among patients with functional psychoses. Second, we wish to further explore the meaning of HPA axis disorder among these patients. If the DST owes its predictive qualities purely to its diagnostic specificity, then diagnosis should have little prognostic significance among nonsuppressors because nonsuppression should, in all

or nearly all cases, indicate true affective disorder. In fact, our earlier study (22) did not support this conclusion: diagnosis was as important among nonsuppressors as it was among suppressors. If nonsuppression predicts better outcomes for reasons other than, or in addition to, its diagnostic specificity, then suppressor status should be similarly predictive within each diagnostic group. Previous findings were more consistent with this pattern, although sample sizes limited conclusions (22). Finally, if the situation is more complex, nonsuppression may occur for one set of reasons among patients with schizophrenia and for other reasons in other patients. Nonsuppression might occur with substantial frequency, but have little prognostic significance, among patients with narrowly defined schizophrenia. Nonsuppression was present in eight of 31 schizophrenic patients described earlier (22), and only a trend indicated prognostic importance. In summary, patterns apparent in our earlier study tended to support the second interpretation described earlier, but conclusions were tentative pending replication.

METHOD

Subject recruitment for the previously described series (1, 22) began in June 1982 and ended in June 1985. The recruitment of a large series described by Schlessner et al. (5) ended in 1979. The intervening period was marked by clinical enthusiasm for the DST, and it was often ordered by treating physicians at our facility. The patients described in this paper, therefore, represent a study group of convenience, and the timing of these other studies determined the length of the follow-up.

We screened inpatient records at a university psychiatric hospital to find those with the following characteristics: a discharge date between December 1979 and December 1982, inclusive; a discharge diagnosis of schizophrenia, schizoaffective disorder, or major depression with psychotic features; no differential diagnosis of an organic mental disorder or mental retardation; documentation of delusions or hallucinations during the episode leading to the index hospitalization; a record of postdexamethasone cortisol values obtained at 8:00 a.m. and/or 4:00 p.m. after 1 mg of dexamethasone given at 11:00 p.m.; and the absence of any medical or pharmacological factors confounding interpretation of the DST (23). This yielded a potential subject pool of 92. Because *DSM-III* criteria for major depression specified the absence of previous mania or hypomania, and because we screened only charts with this diagnosis, this is a unipolar patient group. However, chart review revealed that one of the patients had had a probable history of mania, and this subject was retained.

Raters experienced in the structured interview of psychotic inpatients attempted to locate these individuals for follow-up. Seven (7.6%) had died and another seven could not be located. Of the remaining 78, five (6.4%) refused and two (2.6%) were not interviewable. Thus,

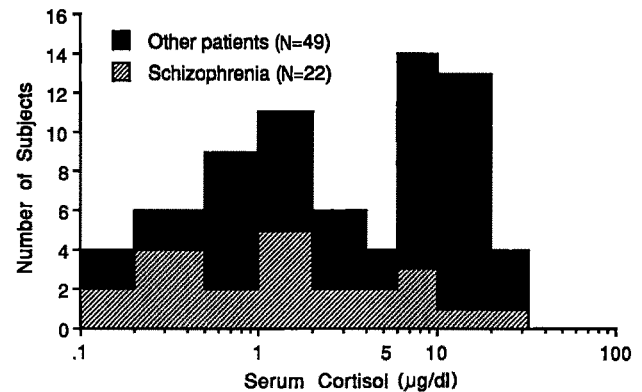
71 (83.5%) of those not known to be dead were successfully followed up. Sixty-four (90.1%) of the interviews were conducted in person, and four (5.6%) were conducted by telephone. Available medical records and interviews with informants provided sufficient information to assess outcome in the remaining three (4.2%) patients. Those who were interviewed on follow-up did not differ significantly from the other patients by sex or postdexamethasone cortisol values. Those lost to follow-up (including those who had died) were significantly older, however (46.2 years, $SD=19.1$, versus 33.9 years, $SD=12.5$; $t=2.8$, $df=25.3$, $p=0.01$).

Follow-up raters were blind to baseline diagnosis and DST results but were aware of the baseline psychotic features. These symptoms were tracked longitudinally to determine whether and when recovery from psychosis had occurred. Questions then focused on the preceding 3 years to determine the nature and persistence of both psychotic and depressive symptoms, the presence or absence of substance abuse, and any history of suicide attempts. The preceding year was reviewed to determine the optimum Global Assessment Scale (GAS) score (24) and to apply outcome scales proposed by Strauss and Carpenter (25). Attention was finally directed to the preceding month to further characterize ongoing affective or psychotic symptoms, to record any psychotropic drugs currently used, and to rate the overall level of psychosocial adjustment as described in the Longitudinal Interval Follow-Up Evaluation (26). In addition, raters obtained medical records pertaining to psychiatric admissions and outpatient psychiatric contacts. Their final judgments as to course and outcome reflected a synthesis of interview and medical record information.

Strauss and Carpenter (25) used five-point scales to rate outcome in four different realms: duration of non-hospitalization for psychiatric disorder, social contacts, usefully employed (including work as housewife or student), and absence of symptoms. A score of 0 corresponded to the worst outcome in each of these areas. Such a score indicated, respectively, that the subject had been hospitalized more than 9 months in the preceding year, did not meet with friends at all under any conditions, had no useful work, or had had continuous and severe signs and symptoms. A score of 4 indicated, respectively, no hospitalization in the preceding year, meetings with friends on the average of at least once a week, employed continuously, or no signs or symptoms.

The Longitudinal Interval Follow-Up Evaluation (26) global rating of psychosocial adjustment used a five-point scale to qualify functioning; a score of 1 indicated a good level of overall adjustment, while a score of 5 indicated poor adjustment or severe impairment. Recovery from affective disorder also reflected Longitudinal Interval Follow-Up Evaluation conventions and required at least 2 continuous months with no more than one or two symptoms to no more than a mild degree. Recovery from psychosis required a minimum of 2 months without delusions or hallucinations and with full insight into preexisting psychotic features.

FIGURE 1. Log-Transformed Maximum Post-DST Cortisol Values of 71 Psychotic Patients



One of us (D.T.), blind to follow-up results, reviewed all available medical records applicable to the hospitalization during which the index DST was obtained or to any earlier hospitalization. This rater noted the extent and nature of all affective and psychotic symptoms and applied diagnostic criteria according to Research Diagnostic Criteria, *DSM-III*, and *DSM-III-R*. To facilitate comparisons to the earlier study (22), this analysis used three major diagnostic groupings according to *DSM-III* criteria. The first contained all patients with major depression and mood-congruent psychotic features, and the second was a nosologically intermediate group consisting of all patients with major depression and mood-incongruent psychotic features, schizophreniform disorder, or schizoaffective disorder. The third was composed of all patients with schizophrenia.

When the results of more than one DST were available, only the first was used. These were performed within 4 days of admission for 39 patients and later in the hospitalizations for the other 32 patients. An 8:00 a.m. sample was available for 68 of the patients and a 4:00 p.m. sample for 64; for 61 patients, both 8:00 a.m. and 4:00 p.m. samples were obtained.

RESULTS

The mean and median lapses between admission and the index DST were 7.9 ($SD=9.2$) and 4 days, respectively. The mean postdexamethasone value for samples drawn within 4 days of admission was not significantly higher than that for samples obtained later, and the two groups had similar nonsuppression rates ($N=18$ of 39, or 46.2%, and 14 of 32, or 43.8%, respectively).

The index postdexamethasone cortisol values assumed a clearly bimodal distribution with a point of rarity clearly within the range of values usually used to separate normal from abnormal DST results (figure 1). In the previous study (22), a larger proportion of patients fell in the ambiguous range between 4 µg/dl and 6 µg/dl, and those patients made up a separate group in the data analysis. Because only four patients in the pres-

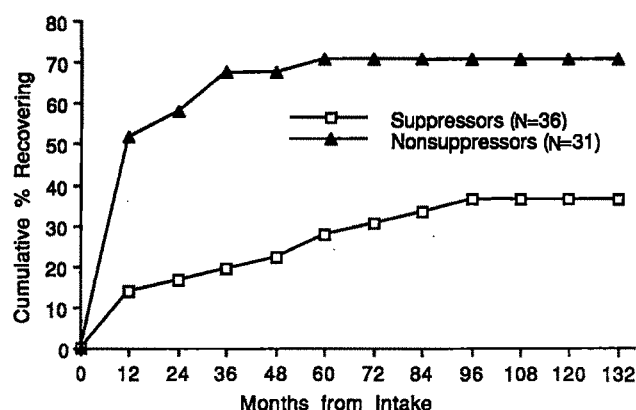
TABLE 1. Age and Length of Illness of 67 Psychotic Patients by Baseline DST Result^a

Item	Suppressors (N=36)		Nonsuppressors (N=31)	
	Mean	SD	Mean	SD
Age at index hospitalization (years) ^b	30.6	10.6	38.2	13.8
Age at onset of illness (years) ^b	24.0	8.1	30.2	11.3
Length of episode (weeks) ^c	55.3	81.1	19.8	28.9

^aData not included for four patients with post-DST cortisol values of 4–6 µg/dl.

^b $t=-2.6$, $df=65$, $p=0.01$.

^c $z=-2.15$, $p=0.03$, Wilcoxon rank sum test.

FIGURE 2. Recovery From Index Psychotic Episode of 67 Patients by Baseline DST Result^a

^aData not included for four patients with post-DST cortisol values of 4–6 µg/dl. Wilcoxon $\chi^2=14.1$, $df=1$, $p=0.0002$.

ent study had cortisol values in this range, they were omitted from categorical comparisons of suppressors (maximum postdexamethasone cortisol less than 4 µg/dl, N=36) and nonsuppressors (maximum postdexamethasone cortisol greater than 6 µg/dl, N=31).

Nonsuppressors had had significantly shorter episode durations than suppressors and were significantly older at intake and at the onset of illness (table 1). The majority in both groups were women (N=21, or 58.3% of suppressors and 19, or 61.3% of nonsuppressors). Nonsuppression occurred in 12 (70.6%) of the 17 patients with major depression and mood-congruent psychotic features, seven (50.0%) of the 14 patients with major depression and mood-incongruent psychotic features, four (36.4%) of the 11 patients with *DSM-III* schizoaffective disorder, three (60.0%) of the five patients with schizophreniform disorder, and five (25.0%) of the 20 patients with schizophrenia.

Three (8.3%) of the 36 patients who had been suppressors and 13 (41.9%) of 31 who had been nonsuppressors eventually recovered with insight ($\chi^2=10.3$, $df=1$, $p=0.001$). Life-table analyses showed that this difference developed early during follow-up (figure 2).

TABLE 2. Psychometric Scale Scores of 67 Psychotic Patients After 8 Years by Baseline DST Result^a

Measure	Suppressors (N=36)		Nonsuppressors (N=31)	
	Mean	SD	Mean	SD
Depressive symptoms in previous month	2.4	2.4	1.9	2.3
GAS score ^b	46.3	11.4	54.5	16.5
Outcome scale scores				
Nonhospitalization in past year ^c	2.7	1.6	3.4	1.1
Absence of symptoms in past month ^d	1.9	1.2	2.6	1.2
Social contacts in past year	2.3	1.3	2.7	1.4
Employment in past year ^e	1.4	1.6	2.6	1.7
Longitudinal Interval Follow-Up Evaluation overall psychosocial adjustment score (rater's judgment) ^f	3.8	0.8	3.2	1.1

^aData not included for four patients with post-DST cortisol values of 4–6 µg/dl.

^b $t=-2.4$, $df=65$, $p=0.02$.

^c $t=-2.1$, $df=65$, $p=0.04$.

^d $t=-2.5$, $df=65$, $p=0.01$.

^e $t=-2.8$, $df=65$, $p=0.007$.

^f $t=2.7$, $df=65$, $p=0.009$.

Outcomes as reflected in GAS scores and in ratings of time in the hospital, employment, number of symptoms, and overall psychosocial adjustment also significantly favored those who had been nonsuppressors (table 2). As anticipated (3), patients with major depression and mood-congruent psychotic features were much more likely to recover than were patients with schizophrenia. Patients with major depression and mood-incongruent psychotic features, schizophreniform disorder, or schizoaffective disorder held intermediate positions (table 3).

DST results had the greatest prognostic importance within the latter group. Among these patients, suppressors and nonsuppressors differed significantly by mean GAS scores (47.9, SD=11.4, and 57.9, SD=12.4, respectively; $t=-2.3$, $df=28$, $p=0.03$). GAS scores did not differ significantly by suppressor status among patients with major depression and mood-congruent psychotic features (52.2, SD=15.5, and 56.3, SD=21.3, respectively) or among patients with schizophrenia (42.7, SD=9.2, and 40.8, SD=3.6, respectively). Among patients with major depression and mood-incongruent psychotic features, none of the seven suppressors, but four of the seven nonsuppressors, were recovered at follow-up ($p=0.03$, Fisher's exact test). On the other hand, none of the patients with *DSM-III* schizoaffective disorder had recovered although four had been nonsuppressors. Of the four schizophreniform patients, one of the two suppressors recovered, as did one of the two nonsuppressors.

Predicted relationships between duration and outcome also emerged. Baseline DST results were related to outcome when episode durations were 1 year or less;

TABLE 3. Recovery of 67 Psychotic Patients After 8 Years by Baseline Diagnosis and DST Result^a

Baseline Diagnosis	Total N	Suppressors			Nonsuppressors		
		N	Recovered ^b		N	Recovered ^c	
			N	%		N	%
Major depression with mood-congruent psychotic features (A)	17	5	2	40.0	12	8	66.7
Major depression with mood-incongruent psychotic features or schizophreniform or schizoaffective disorder (B) ^d	30	16	1	6.3	14	5	35.7
Schizophrenia (C)	20	15	0	0.0	5	0	0.0

^aData not included for four patients with post-DST cortisol values of 4–6 µg/dl.

^bA versus B versus C: $p=0.04$ (Fisher's exact test); A>C: $p=0.05$ (Fisher's exact test).

^cA versus B versus C: $p=0.03$ (Fisher's exact test); A>C: $p=0.02$ (Fisher's exact test).

^dSuppressors versus nonsuppressors: $p=0.05$ (Fisher's exact test).

three of the 26 suppressors (11.5%) and 13 of the 28 nonsuppressors (46.4%) with these durations recovered ($\chi^2=7.9$, $df=1$, $p<0.005$). None of the patients with longer episode durations recovered, even though three had been nonsuppressors.

Also as expected, a later age at onset was associated with a higher likelihood of recovery; the mean age at onset was 25.2 years ($SD=8.5$) for those who did not recover and 32.2 years ($SD=13.0$) for those who did (Wilcoxon rank sum test, $z=2.06$, $p=0.04$). Current age was not a significant predictor of recovery.

Because age at onset, episode duration, and diagnosis were each associated both with the likelihood of recovery and with postdexamethasone cortisol values, they were entered into a logistic regression analysis with recovery as the dependent variable (table 4). With episode duration, diagnosis, and age at onset in the model, suppressor status remained a significant predictor of outcome. The significant relationship between suppressor status and outcome also persisted in a logistic regression analysis from which the 20 schizophrenic patients were excluded. Age at onset was not a significant predictor among nonschizophrenic patients and was therefore not included in this model.

One of the four patients with postdexamethasone cortisol values in the ambiguous range (4–6 mg/dl, inclusive) was recovered from psychosis at follow-up. Six (46.2%) of the 13 patients with values greater than 6 µg/dl but less than 10 µg/dl were recovered, while seven (38.9%) of the 18 with values greater than 10 µg/dl recovered. These data did not suggest an optimal threshold for predicting recovery other than the conventional one approximating 5 µg/dl.

DISCUSSION

DST results among the psychotic inpatients were strongly associated with outcome on follow-up. In this regard, these data clearly confirm our earlier findings (22) and increase the likelihood that this relationship is generalizable. The two studies also concur in finding an interdependence between DST results and diagnosis in the prediction of outcome; nonsuppressors who had major depression had much better outcomes than did nonsuppressors who had schizophrenia. Thus, the prog-

TABLE 4. Logistic Regression Analysis of Baseline Measures and Recovery of Psychotic Patients After 8 Years

Model and Variable	Likelihood Ratio Test, χ^2 ($df=1$)	p
Model 1 ^a		
Episode duration	9.39	0.002
Diagnosis (schizophrenia versus others)	4.96	0.03
Age at onset	0.90	0.34
Suppressor status	5.22	0.02
Model 2 ^b		
Episode duration	6.95	0.008
Diagnosis (major depression with mood-congruent psychotic features versus others)	2.95	0.09
Suppressor status	4.89	0.03

^a $\chi^2=30.4$, $df=4$, $p<0.0001$, $R=0.55$, $N=67$.

^b $\chi^2=19.1$, $df=3$, $p=0.0003$, $R=0.47$, $N=47$ (schizophrenic patients excluded).

nostically favorable significance of DST nonsuppression cannot be attributed solely to its diagnostic specificity. The situation is apparently more complex.

In both studies DST nonsuppression occurred among patients with a diagnosis of schizophrenia, but in neither was suppressor status significantly associated with outcome among schizophrenic patients. What, if anything, does DST nonsuppression signify in schizophrenia? While some researchers have failed to find clinical differences between schizophrenic patients who are DST suppressors and schizophrenic patients who are DST nonsuppressors, those who have consistently noted that nonsuppressors were more likely to have disorganized (27) or type II (13, 14) schizophrenia or were less likely to have positive symptoms (9). In the present study as well, patients with disorganized or hebephrenic schizophrenia were more likely to be nonsuppressors than were other schizophrenic patients (two of five, or 40%, versus two of 13, or 15.4%). Disorganized or type II forms of schizophrenia, in turn, have been associated with higher ventricle-brain ratios (28) and with cognitive deficits (29, 30) which may be quite severe (31). The fact that patients with dementia also have substantial rates of DST nonsuppression (32) invites speculation that a process common to chronic, type II schizophrenia and to irreversible dementia may give rise to DST nonsuppression in these conditions.

The correlates of DST nonsuppression in the affective disorders indicate a different underlying mechanism. Nonsuppression among depressed patients has been most consistently associated with severity, as reflected in endogenous, psychotic, or seriously suicidal features (33). Moreover, the clinical phenomena characteristic of patients with affective syndromes and atypical psychotic features (schizoaffective disorder or major depression with mood-incongruent psychotic features) suggest that it is type I and not type II schizophrenia that is liable to inclusion in these groups. In two large series, patients with Research Diagnostic Criteria (34) schizoaffective depression rarely exhibited blunted or inappropriate affect or formal thought disorder (18, 35). If, as these data suggest, type II schizophrenic patients are seldom misdiagnosed as having affective or schizoaffective disorders, they will be found only among patients who meet strict criteria for schizophrenia. Therefore, DST nonsuppression may be highly specific to true affective disorder among psychotic patients only after those who meet narrow definitions of schizophrenia have been excluded.

Notably, however, the distinctions between major depression with mood-congruent psychotic features on the one hand, and schizoaffective disorder or major depression with mood-incongruent psychotic features on the other, were prognostically important among DST nonsuppressors as well as among DST suppressors. While some cell sizes were quite small, the overall patterns here closely resembled those of our earlier study (22). This suggests that there are two reasons for the relatively poor prognoses regularly seen among depressed patients with mood-incongruent psychotic features (36). Some of these patients may not have affective disorder but may instead have schizophrenia; this view is supported by much repeated family history findings (3). Among those who do not have schizophrenia, however, mood-incongruent psychotic features may indicate a relatively persistent and disabling form of true affective disorder.

While we expected the differences we found in recovery rates by diagnosis and DST status, we did not expect overall rates to be as low as they were. Our earlier study (22) recruited patients from the same facility and employed the same diagnostic criteria and the same definition of recovery on follow-up. Yet that study found that recovery had occurred after only 1 year in 17 (70.8%) of 24 patients with major depression with mood-congruent psychotic features, 14 (45.2%) of 31 patients with major depression with mood-incongruent psychotic features, and four (12.9%) of 31 patients with schizophrenia. Corresponding figures in the present study were 10 (58.8%) of 17, six (20.0%) of 30, and none of 20, respectively. Thus, recovery rates were lower in each diagnostic group despite a much lengthier follow-up period. We cannot account for these differences across studies. However, the fact that the same outcome predictors emerged in both studies (episode duration, *DSM-III* diagnosis, and DST result) indicates that outcome ratings were reliable and valid.

Both the present results and those of the first series (22) support the following approach to prognosis in patients with nonmanic psychosis. A narrowly defined diagnosis of schizophrenia implies a low likelihood of full recovery; DST results may be prognostically meaningless for these patients, or nonsuppression may even portend a worse prognosis. Patients who have *DSM-III* diagnoses of major depression with mood-congruent psychotic features, major depression with mood-incongruent psychotic features, or schizoaffective disorder have, as a group, better outcomes than those who meet criteria for schizophrenia. Among these patients, however, those with abnormal DST results (nonsuppressors) have significantly better outcomes than those with normal DST results.

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The Dexamethasone Suppression Test in Adolescent Outpatients With Major Depressive Disorder

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Objective: The purpose of the study was to determine whether the dexamethasone suppression test (DST) would discriminate between outpatient adolescents with major depressive disorder and normal adolescent comparison subjects. **Method:** Depressed patients were accepted into the study only if they fulfilled the Research Diagnostic Criteria for major depressive disorder. The depressed subjects (N=44) and the normal subjects (N=38) were studied in the same environment and under the same conditions. The subjects received 1 mg of dexamethasone at 11:00 p.m. The next day, blood for determining plasma cortisol concentrations was drawn through an indwelling catheter every 60 minutes from 8:00 a.m. until 11 p.m. **Results:** After dexamethasone, the cortisol levels of the adolescents with major depressive disorder and the normal subjects were not significantly different. Only six (14%) of the depressed subjects and one (3%) of the normal subjects showed evidence of nonsuppression (cortisol value greater than 5 µg/dl). Analyses of subgroups of the depressed patients based on suicidal tendencies and endogenous subtype also failed to reveal significant differences in cortisol values. Estimates of the severity of depression showed significant negative correlations with cortisol values among the depressed patients. **Conclusions:** In contrast with previous studies of adolescent inpatients, the DST did not discriminate between the adolescent outpatients with major depressive disorder and the normal comparison subjects in this study. Possible reasons for the discrepancies, such as severity of the depression and inpatient status, are discussed.

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There has been controversy concerning the role of the dexamethasone suppression test (DST) as a tool for the diagnosis of major depressive disorder in adults, children, and adolescents. Casat et al. (1) reviewed the available studies on the use of the DST in children and adolescents. There were eight studies on adolescents (2-9), with a total of 475 inpatients, of whom 157 (33%) had major depressive disorder. These studies used a prospective design, the Research Diagnostic Criteria, or *DSM-III* criteria for diagnosis and included one or more control groups. In all of them, 1 mg of dexamethasone was administered at 11:00 p.m. In most of the studies, blood samples for determination of cortisol levels were drawn at 4:00 p.m. and 11:00 p.m.

on the day after dexamethasone administration. Casat et al. showed that 74 (47%) of the adolescent inpatient subjects with major depressive disorder and 63 (20%) of the subjects with other psychiatric disorders were nonsuppressors of cortisol ($\chi^2=3.84$, $df=1$, $p<0.0001$). When a serum cortisol level of 138 nmol/liter (5 µg/dl) was used as the threshold for nonsuppression, the pooled DST sensitivity and specificity were 47% and 80%, respectively.

Our study adds uniquely to the existing literature on the DST in adolescent major depressive disorder by virtue of the following four main features. 1) It used a large *outpatient* group of depressed adolescents. 2) Both depressed and normal subjects were studied in the same environment and under the same conditions. 3) After administration of dexamethasone, cortisol levels were determined each hour from 8:00 a.m. to 11:00 p.m. (i.e., 16 times) from blood drawn through an indwelling venous catheter. 4) The majority of these adolescent subjects had also participated in another study of 24-hour baseline cortisol measures, permitting within-subject comparisons of 24-hour baseline cortisol levels with DST cortisol levels.

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METHOD

Patients were accepted for screening at a child and adolescent depression clinic if they were reported to appear sad, said they felt sad, had suicidal ideation or behavior, were nervous or afraid, or displayed ritualistic behavior. After informed consent was obtained, each patient was screened for appropriateness for the study in a 10- to 14-day diagnostic evaluation that included, in the following order, the Schedule for Affective Disorders and Schizophrenia for School-Age Children, Present Episode (KIDDIE-SADS-P) (10), the Psychosocial Schedule (11), a pediatric history and examination including Tanner staging (12, 13), and, 10–14 days later, another KIDDIE-SADS-P covering the past week. The second KIDDIE-SADS-P assessment was done without knowledge of the findings of the first. The diagnosis of major depressive disorder was made with the unmodified adult Research Diagnostic Criteria (RDC) (14). The diagnoses of nonaffective emotional disorders conformed to *DSM-III* criteria.

All subjects were between the ages of 11 and 18 years and had reached at least Tanner stage III of sexual development, as determined by a pediatrician. Depressed subjects were accepted into the study only if they fulfilled the RDC for major depressive disorder (at least probable) in both KIDDIE-SADS-P evaluations. Major depressive disorder was considered to be endogenous only if it fulfilled the RDC for definite endogenous subtype in both evaluations. If not, subjects were classified as having the nonendogenous subtype.

Potential subjects were excluded if they met any of the following criteria: 1) use of psychoactive medication that could affect hypothalamic-pituitary function, 2) significant physical illness, especially endocrinopathies or heart disease, 3) obesity (weight-for-height greater than 95% on the National Center for Health Statistics curve) or growth failure (height or weight lower than the third percentile), 4) clinically diagnosed seizures or other major neurological illness, 5) IQ less than 70, 6) fulfillment of the *DSM-III* criteria for anorexia nervosa, autism, or schizophrenia, and 8) inordinate fear of needles (needle phobia).

Normal comparison subjects were recruited through personal contacts and informal networking. The exclusion criteria enumerated above were also used for this group. The criterion for inclusion was no current or past history of child psychiatric disorder, as determined by a single KIDDIE-SADS-E assessment (mother and child interviewed independently).

Eighty-two subjects were accepted for the study: 44 patients with major depressive disorder (24 had the endogenous subtype, 19 were suicidal, and four were psychotic) and 38 normal comparison subjects. Two of the subjects had more than two missing data points at the end of the testing and were dropped from the study. There were no significant group differences in age (patients with major depressive disorder: mean=14.9 years, SD=1.9; normal subjects: mean=15.3 years, SD=1.5), sex (patients: 22 female and 22 male; normal sub-

jects: 13 female and 25 male), or race (patients: 28 white, six black, and 10 other; normal subjects: 21 white, eight black, and nine other).

Severity of depression was assessed by examining scores on the KIDDIE-SADS-P and by extracting scores on the 21-item Hamilton Rating Scale for Depression from the KIDDIE-SADS-P scores with an adaptation of the method of Endicott et al. (15). The mean Hamilton depression score for the patients with major depressive disorder was 24.7 (SD=4.3). There was no statistically significant difference in Hamilton depression scores between patients with endogenous major depression (mean=25.2, SD=5.0) and those with nonendogenous depression (mean=24.1, SD=3.1) ($t=0.87$, $df=39$, $n.s.$). The patients with suicidal ideation (score of 4 or more on the KIDDIE-SADS-P item for suicide, indicating a definite plan or attempt) tended to have higher Hamilton depression scores (suicidal, mean=26.1, SD=5.0; not suicidal, mean=23.7, SD=3.4) ($t=1.86$, $df=41$, $p=0.07$). There were significant differences in Hamilton depression scores between the male and female depressed patients (male, mean=23.3, SD=4.3; female, mean=26.2, SD=3.7) ($t=2.35$, $df=41$, $p=0.02$).

After the 2-week diagnostic protocol and acceptance into the study, subjects came to a sleep/neuroendocrine unit to be tested. An indwelling catheter was placed in an antecubital vein, and the vein was kept open by a slow drip of heparinized saline. Blood samples were immediately centrifuged, and the plasma was separated and then frozen.

Plasma cortisol was analyzed by competitive protein-binding radioassay with intra-assay coefficients of variation of 9.1%, 3.7%, and 2.4% at 68.9, 342.1, and 557.3 nmol/liter, respectively, and interassay coefficients of variation of 9.6%, 3.9%, and 4.8% at the same levels.

This study was part of a psychobiological study of children with major depressive disorder that included the following general neuroendocrine and sleep measures: night 1: sleep EEG; day 1: thyrotropin-releasing hormone (TRH) challenge tests; night 2: sleep EEG; day 2: 24-hour test of blood cortisol levels; night 3: sleep EEG; day 3: morning, insulin tolerance test; 3:00 p.m., amphetamine challenge test; 11:00 p.m., administration of 1 mg p.o. of dexamethasone; day 4: testing of blood cortisol levels hourly from 8:00 a.m. until 11:00 p.m. Approximately 90% of the subjects participated in the full protocol. The other 10% participated only in the amphetamine challenge test and the DST. There was no difference in DST results between the latter subjects and those who participated in the full protocol.

A subgroup of 14 subjects (eight patients with major depressive disorder and six normal subjects) participated in an earlier version of the DST protocol with the indwelling catheter, but plasma sampling was done only at 8:00 a.m., 4:00 p.m., and 11:00 p.m. The data of these subjects were included only in the analyses of those time points. Thus, for the 16-hour analysis we included data on only 66 subjects: 35 patients with major depressive disorder (19 endogenous, 16 suicidal,

TABLE 1. Postdexamethasone Plasma Cortisol Levels of Adolescents With Major Depressive Disorder and Normal Adolescent Comparison Subjects

Cortisol Measure (nmol/liter)	Depressed Patients		Normal Subjects		Mann-Whitney U	p
	Mean	SD	Mean	SD		
Mean 16-hour ^a	28.9	34.4	22.0	19.7	568	0.74
Peak ^a	77.3	82.8	65.1	64.3	564	0.79
8:00 a.m. ^b	35.8	61.4	17.7	11.6	858	0.84
4:00 p.m. ^b	34.6	52.1	21.9	25.0	894	0.59
11:00 p.m. ^b	28.5	36.1	27.4	35.5	877	0.70
Mean (8:00 a.m., 4:00 p.m., and 11:00 p.m.) ^b	33.0	41.5	22.3	18.7	— ^c	0.38

^aFor depressed patients, N=35; for normal subjects, N=31.

^bFor depressed patients, N=44; for normal subjects, N=38.

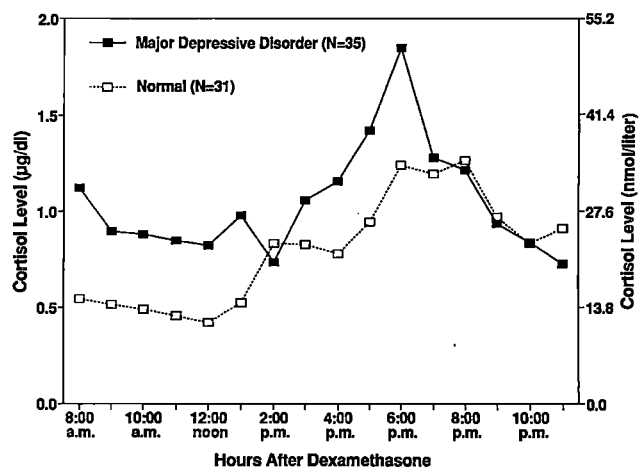
^ct=0.89, df=80.

three psychotic) and 31 normal comparison subjects. This subgroup of subjects (hereafter referred to as the "reduced group") participated in all of the studies we have described, and the protocol was in all other ways identical to that for the rest of the group. As in the full group of subjects, there were no significant differences in age, sex, or race between the depressed patients and the normal subjects in the reduced group.

In the statistical analysis, cortisol levels were examined for normality with the W statistic of Shapiro and Wilk (16) and transformed as necessary before testing with parametric techniques. If, after transformation, the measures were still significantly abnormal, non-parametric techniques (e.g., the Mann-Whitney test) were used for between-group comparisons. Spearman correlation coefficients were used to examine the associations between cortisol levels and severity of depression. The problem of missing data was minimal. The two subjects who had more than two consecutive missing samples were excluded from all examinations of the mean 16-hour cortisol levels. One or two missing samples from a single subject were linearly interpolated.

RESULTS

After the administration of dexamethasone, there were no significant differences between the depressed group and the normal group on the following summary variables: mean 16-hour cortisol level, peak cortisol level, and mean cortisol level measured at each of the 16 testing times, including cortisol levels for "standard" testing times (8:00 a.m., 4:00 p.m., and 11:00 p.m.) (table 1, figure 1). Repeated measures analysis of variance with the Greenhouse-Geisser adjustment (17) showed a significant effect of time ($F=4.4$, $df=4.4$, 284.4 , $p=0.002$) but not a significant Time by Diagnosis interaction ($F=1.05$, $df=4.4$, 284.4 , $p=0.40$). There was no significant difference between the depressed patients and the normal subjects in the percentage of samples with cortisol values of 138 nmol/liter (5 μ g/dl) or more. These summary cortisol variables and the percentage of

FIGURE 1. Sixteen-Hour Postdexamethasone Plasma Cortisol Levels of Adolescents With Major Depressive Disorder and Normal Adolescent Comparison Subjects

samples with cortisol values of 138 nmol/liter or more also failed to discriminate among the subgroups of patients with major depressive disorder (suicidal, endogenous, and psychotic). Contrary to our expectation that patients with more severe depression would show higher postdexamethasone plasma levels of cortisol, we found a *negative* correlation between severity of depression and mean 16-hour cortisol level ($r_s=-0.46$, $N=34$, $p=0.006$), peak cortisol level ($r_s=-0.50$, $N=34$, $p=0.003$), 4:00 p.m. cortisol level ($r_s=-0.43$, $N=43$, $p=0.004$), 11:00 p.m. cortisol level ($r_s=-0.30$, $N=43$, $p=0.06$), and mean cortisol level for blood samples taken at 8:00 a.m., 4:00 p.m., and 11:00 p.m. ($r_s=-0.40$, $N=43$, $p=0.02$).

Exploratory analyses of covariance revealed no significant effects of age, sex, or the Age by Sex and Age by Diagnosis interactions on any of the summary cortisol variables for the full study group. Within the reduced group, the female subjects had significantly higher hourly and mean 16-hour postdexamethasone cortisol levels than the male subjects (female: mean=28.1 nmol/liter, $SD=19.3$; male: mean=23.9 nmol/liter, $SD=33.5$) ($U=705$, $p<0.02$).

In addition to the continuous variable analyses, we explored categorical comparisons of our data with data from clinically based studies that used the concept of a cutoff value to indicate nonsuppression of cortisol. We chose a standard cutoff of 138 nmol/liter (5 μ g/dl) at any of the three usual time points (8:00 a.m., 4:00 p.m., and 11:00 p.m.) to define nonsuppression. This revealed that six of the 44 patients with major depressive disorder were nonsuppressors, compared to one of the 38 normal subjects ($p<0.20$, Fisher's exact test). Comparison of clinical variables (Hamilton depression scores, endogenous subtype, sex, suicidality, and age) between the nonsuppressors ($N=6$) and the rest of the group with major depressive disorder ($N=38$) revealed no significant differences.

Approximately 90% of the subjects in this research

also participated in a study of 24-hour baseline cortisol secretion. In that study, Dahl et al. (18) reported no significant differences in the peak, nadir, or time of the nocturnal rise of plasma cortisol between patients with major depressive disorder and normal subjects. We examined the relation between the mean 24-hour baseline cortisol levels from that study and the postdexamethasone mean 16-hour cortisol levels in this study and found a significant positive correlation ($r_s=0.54$, $N=64$, $p<0.0001$).

We used receiver operating characteristic analysis (19) to explore the sensitivity and specificity of the DST. This curve is a standard way of showing the various possible pairs of test sensitivity (rate of true positives) and specificity (1 minus the rate of false positives) at various cutoff scores. We analyzed the mean 16-hour, peak, 8:00 a.m., and 4:00 p.m. cortisol values for 100 cutoff scores (from 0.0 nmol/liter to 220.7 nmol/liter). All of the receiver operating characteristic curves obtained were not significantly different from the expected random receiver operating characteristic curve. (Figure 2 shows the receiver operating characteristic curve for cortisol values at 4:00 p.m.) For comparison with other studies, we also used 138 nmol/liter (5 $\mu\text{g/dl}$) as the cutoff cortisol value to define nonsuppression. With this cutoff level, the sensitivity and specificity for 8:00 a.m. and 4:00 p.m. were 9.0% and 100%, respectively. Sensitivity and specificity were identical when 4:00 p.m. values were used.

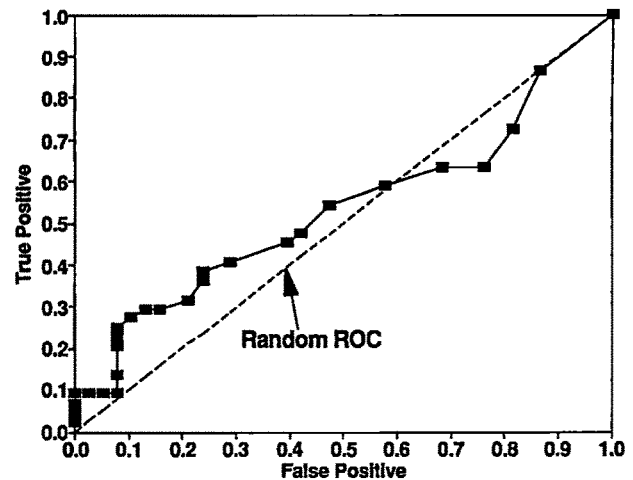
DISCUSSION

In contrast with previous *inpatient* adolescent studies, the DST in our sample of outpatients did not discriminate between patients with major depressive disorder and normal comparison subjects. Similarly, our group has also reported (20) that in a large group of prepubertal subjects with major depressive disorder (predominantly outpatients), the DST did not discriminate among subjects with major depressive disorder, those with nonaffective psychiatric disorders, and normal subjects.

The reason for these discrepancies with previous reports on inpatients is not clear. Possible factors contributing to positive findings with inpatient subjects include 1) severity of depression in the subjects being studied and 2) stress induced by the hospitalization.

In adults, high rates of DST nonsuppression are associated with greater scores on severity of depression (21). Because of this association, one must consider possible differences in severity as contributing to the negative results in this study. Our results in adolescents do not support this explanation. Our overall study group had Hamilton depression scale scores indicating moderate to high severity. Further, in contrast with the reports on the DST with adults, the correlation between severity scores and post-DST cortisol levels was *negative*. Thus, it appears unlikely that severity is the sole answer to these discrepancies, at least in the adolescent age group.

FIGURE 2. Receiver Operating Characteristic (ROC) Curve for Post-dexamethasone Plasma Cortisol Levels at 4:00 p.m. in Adolescents With Major Depressive Disorder and Normal Adolescent Comparison Subjects



We believe that a second important source of variance, potentially contributing to differences between the results of our studies and the existing literature on depressed inpatient adolescents, is the stress of hospitalization. The relatively low-stress environment in our sleep laboratory (to which the adolescents had adapted during the psychobiological protocols) may not have been sufficient to uncover a vulnerability to stress associated with depression. In previous studies, the stress of being on an inpatient unit may have contributed to the positive DST findings.

Stress such as surgery, preoperative surgery procedures, examinations, and admission to the hospital may trigger a large transient rise in cortisol production (for reviews of this subject see 22, 23). To our knowledge there are no studies of adolescents that have directly addressed this issue. The few studies of children have shown the same trends. For example, Tennes and Kreye (24) showed that grade-school subjects had significantly higher urinary cortisol levels on mornings when classroom examinations were scheduled than on other days. Knight et al. (25) demonstrated that children, particularly those who denied stress, had significantly increased urinary cortisol secretion after admission to the hospital for elective surgery. Barnes et al. (26), studying children undergoing open heart surgery, found that urinary 17-hydroxycorticosteroids were significantly elevated on the day before surgery and on the day of return from intensive care.

It is likely that stress increases the rate of nonsuppression of cortisol after administration of dexamethasone. There are no studies of stress-induced nonsuppression of cortisol on the DST in children or adolescents. In adult psychiatric and medical patients, hospitalization has been found to induce an increase in the rate of nonsuppression on the DST in the first 48 hours after admission (21). Ceulemans et al. (27) administered the DST to 40 presurgical patients and 20 normal control

subjects. They found that all of the control subjects were suppressors, but 47.5% of the presurgical patients were nonsuppressors. Blumenfeld et al. (28) found impaired urinary 17-hydroxycorticosteroid suppression after dexamethasone administration in military trainees under stress. Baumgartner and Kurten (29) showed that depressed patients, schizophrenic patients, and normal volunteers under stress (giving a lecture) had similar rates of cortisol nonsuppression (56.5%, 50.0%, and 43.8%, respectively).

The indwelling catheter itself may also cause stress; however, in this study the blood samples were drawn after subjects had adapted to the laboratory environment and the indwelling catheter. Another group of subjects in the same laboratory, who were following similar protocols, were assessed for stress. They indicated that the degree of subjective stress was quite low and that the indwelling catheter as a rule caused little discomfort (30). In previous studies, subjects experienced the combined stress of repeated venipunctures and the hospitalization process (particularly when the DST was done shortly after admission). In some studies, these combined stresses may have interacted to produce nonsuppression.

In summary, stress increases baseline cortisol levels as well as nonsuppression of cortisol on the DST. It may contribute to the differences in the results of inpatient and outpatient investigations that we have described.

In this study, we found a negative correlation between severity of depression and cortisol level. Thus, patients with high Hamilton depression scores had lower post-DST cortisol levels. This finding is the opposite of what we expected and needs further exploration.

One limitation of this study was that serum dexamethasone levels were not ascertained. Several studies of adults with major depressive disorder have reported a significant negative correlation between cortisol and dexamethasone levels (31–35), suggesting that cortisol nonsuppressors have a lower level of plasma dexamethasone than cortisol suppressors. Naylor et al. (36) studied 73 inpatient children aged 5–14 years and found that overall, DST nonsuppressors had significantly lower plasma dexamethasone levels than suppressors; similar nonsignificant trends were observed in the depressed subjects. In addition, our group (20) studied 24-hour plasma levels of dexamethasone in children with major depressive disorder and found no statistically significant difference in dexamethasone levels between the suppressor and nonsuppressor depressed patients and also no difference between the depressed patients, the patients with nonaffective psychiatric disorders, and the normal subjects.

A second potential limitation of this study was the dose of dexamethasone administered. It is possible that a lower dose might have improved the sensitivity of the DST in this group of patients. However, to our knowledge there have been no studies comparing dexamethasone dosages in adolescents. Only two studies of children have addressed this issue. Doherty et al. (37) investigated dose response and reported that there were

no significant differences in the percentages of children who were nonsuppressors in response to low, medium, and high doses of dexamethasone based on body weight. On the other hand, Naylor et al. (36) did not find a correlation between milligram-per-kilogram dexamethasone dose and plasma dexamethasone concentration, but they did find a significant correlation with body surface area.

Although our data suggest that the DST may not have clinical utility, there may be research value in delineating a biologically distinct subgroup of depressed subjects who do not suppress cortisol on the DST. Particularly with young subjects, the long-term follow-up of this biologically distinct subgroup may provide essential information. Along these lines, we have some follow-up data that concern our subjects, although they did not have systematic clinical follow-up. Rao et al. (38) recently began the process of identifying and following up a wide range of children and adolescents initially studied by the Puig-Antich et al. group, including adolescents from the present study. Rao et al. have located approximately 78% of the subjects with major depressive disorder across studies and have found that eight committed suicide. Three of those eight were subjects in this study, two of whom had shown nonsuppression of cortisol on the DST. Although this is primarily an anecdotal observation (not a statistically significant finding), it is provocative that at least two of the six nonsuppressors committed suicide. This finding is also interesting because of previous reports that suicidal ideation was correlated with high basal cortisol secretion near sleep onset in adolescents with major depressive disorder (39), high urinary free cortisol (40), and nonsuppression of cortisol on the DST (41–45). Controlled longitudinal follow-up studies in combination with the DST and other biological measures will be needed to address this relationship.

In conclusion, both baseline cortisol levels (18) and cortisol levels after dexamethasone in the adolescents we studied failed to show significant group differences, suggesting that the hypothalamic-pituitary-adrenal axis was functionally normal in the overall sample of depressed adolescents. There was a small subgroup of nonsuppressors who did not appear to be clinically distinct from the rest of the group with major depressive disorder. Clinical follow-up of this group may help to delineate the possible role of the DST as a research tool.

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Relapse After Cognitive Behavior Therapy of Depression: Potential Implications for Longer Courses of Treatment

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Objective: The authors studied the risk of relapse among depressed patients after cognitive behavior therapy in order to document the need and potential indications for longer-term models of treatment. **Method:** Forty-eight patients with major depression who responded during a 16-week course of cognitive behavior therapy entered a 1-year prospective follow-up study, as did two patients who received 20 weeks of therapy. Standardized, independent clinical assessments were completed 1, 3, 6, 9, and 12 months after treatment. Relapse was defined as, at minimum, a 2-week period in which the subject met the DSM-III-R criteria for major depression and had a Hamilton depression scale score of 15 or more. **Results:** Sixteen patients (32%) relapsed during the 1-year follow-up. Correlates of relapse included a history of depressive episodes, higher levels of depressive symptoms and dysfunctional attitudes, slower response to therapy, and being unmarried. Patients who fully recovered during therapy (Hamilton depression score of 6 or less for 8 weeks or more) were at significantly lower risk for relapse than those who partially recovered (9% and 52%, respectively). Slower response to therapy, unmarried status, and high residual scores on the Dysfunctional Attitudes Scale were independently and additively related to increased risk of relapse. **Conclusions:** These findings provide further evidence of a relation between residual symptoms and relapse after cessation of active treatment. The authors strongly recommend that models of longer-term psychotherapy be developed for depressed patients who do not recover fully during time-limited cognitive behavior therapy.

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A number of studies over the past 15 years have indicated that cognitive behavior therapy (1) is an effective short-term outpatient treatment of depression (2). Indeed, there is some suggestion that an initial, time-limited course of cognitive behavior therapy may convey additional prophylactic benefits after termination of therapy (3-7). Nevertheless, relapse after termination of acute treatment of depression remains a significant public health problem (8, 9), and, more specifically, the maintenance of therapeutic gains after short-term cognitive behavior therapy is far from complete (3-7). We therefore initiated a prospective, longi-

tudinal study of patients who had been treated with cognitive behavior therapy in the Psychobiology of Recovery in Depression project (10, 11). One goal of the longitudinal study was to document the frequency of relapse during the first year of follow-up as a way of determining whether there is a need for developing longer-term models of cognitive behavior therapy. A second goal was to identify clinical correlates of relapse that might help clinicians to identify patients who would be likely to benefit from such continued therapy. We now report the 1-year outcome and clinical correlates of relapse in a study of 50 patients who responded during time-limited cognitive behavior therapy.

METHOD

The recruitment, screening, assessment, and treatment of outpatients participating in the Psychobiology of Recovery in Depression project protocol have been described in detail elsewhere (10, 11). To summarize briefly, patients were initially evaluated by a team of

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clinician-psychiatrists, and if they met the *DSM-III-R* criteria for major depression, they were seen subsequently by our research team for a secondary evaluation, which included medical history, physical examination, laboratory screening studies (CBC, chemistry screen, and thyroid function tests), and an independent research interview using the Schedule for Affective Disorders and Schizophrenia (SADS) (12) and the 17-item Hamilton Rating Scale for Depression (13).

On the basis of these evaluations, patients were offered enrollment in the study only if they 1) met the Research Diagnostic Criteria (RDC) (14) for a diagnosis of primary major depression (nonbipolar, nonpsychotic subtype) of 18 months' duration or less; 2) met the RDC for probable or definite endogenous subtype; 3) had Hamilton depression scale scores of 15 or more; 4) did not suffer from untreated or poorly controlled conditions that may cause depression (e.g., hypothyroidism), invalidate EEG sleep studies (e.g., sleep apnea), or require treatment with agents that may do either (e.g., β blockers); 5) did not meet criteria for antecedent dysthymia (*DSM-III-R*) or minor or intermittent depressive disorders (14); 6) had no history of active drug or alcohol abuse or dependence (either primary or secondary) during the 2 years before intake into the study; 7) were not judged to have severe intercurrent personality pathology according to *DSM-III-R* criteria (for example, patients with well-established diagnoses of borderline or antisocial personality disorder at the intake interview were excluded); and 8) provided written informed consent. These inclusion and exclusion criteria were designed to yield a homogeneous study group of persons who were in an acute or subacute episode of moderate to moderately severe major depression.

Of more than 130 patients who were evaluated for eligibility, 80 met the entry criteria and 76 enrolled in the study. The two major reasons for exclusion from the protocol were insufficient severity of RDC endogenous features and chronicity of the index episode. Only one potentially eligible patient from this nearly consecutive series of patients newly accepted for therapy refused the protocol in favor of pharmacotherapy; three other potentially eligible patients were referred by the secondary assessment team for immediate (nonresearch) treatment because of marked severity of depression and suicidal tendencies.

After completion of all research assessments, cognitive behavior therapy was begun. The patients received no psychotropic medications during the entire course of treatment. Therapy was conducted according to the manual of Beck et al. (1) with a 16-week, 20-session outpatient protocol (twice-weekly sessions for 4 weeks and weekly sessions thereafter). The therapists had completed at least 2 years of supervised training and had received external certification according to the standards established for use in the National Institute of Mental Health Treatment of Depression Collaborative Research Program (15). Unlike the therapists in the collaborative study, however, the therapists received ongoing weekly supervision.

During the course of treatment, the patients were seen biweekly for independent assessments of symptomatic status according to the Hamilton depression scale, the Beck Depression Inventory (16), and the Global Assessment Scale (GAS) (17). In addition, the Dysfunctional Attitude Scale (unpublished scale by A. Weisman and A.T. Beck, reviewed by Merluzzi and Boltwood [18]) was administered at the beginning and end of the acute treatment protocol. The reliability of the diagnostic measures and clinician-rated scales had been established during a pilot phase of the study and monitored annually according to the standards of our mental health clinical research center (19). Upon completion of the treatment protocol, patients were considered nonresponders if they met the following criteria: 1) less than 50% reduction in Hamilton depression scale score since pretreatment assessment, 2) final Hamilton depression scale score higher than 10, and 3) inability to sustain response for at least 2 weeks by week 16.

Of the first 76 patients to enter the treatment protocol, two (3%) withdrew during the first week of therapy and 10 others (13%) did not complete the entire protocol. The 64 patients who did complete the protocol included 12 (19%) who met the criteria for nonresponders. Alternative treatments were available for these patients. Fifty patients (78% of the completers) had at least 2 consecutive weeks in which their Hamilton depression scale scores were 10 or lower and had 50% or greater reductions from their pretreatment Hamilton depression scores. Forty-eight of these 50 patients enrolled in the follow-up study. Two other patients met the Hamilton depression scale criteria for nonresponse at week 14 but had scores within the responder range at week 16. Both of these patients received 4 additional weeks of therapy and entered the follow-up study after meeting response criteria at week 20.

For the purposes of the follow-up study, we operationalized the definition of Keller et al. (20) for recovery from unipolar depression as follows: a stable reduction of Hamilton depression scale scores to 6 or less for at least 2 months (from weeks 8 through 16 of the treatment protocol). According to this definition, 23 (46%) of the 50 patients who entered the follow-up study were considered recovered; the remaining 27 patients (54%) were classified as partially recovered at the beginning of the follow-up period.

During the first year of follow-up, patients were seen by an independent clinical evaluator 1, 3, 6, 9, and 12 months after treatment. All patients were guaranteed a renewed course of therapy in the event of relapse. Accordingly, patients were encouraged to contact the protocol staff for additional emergency evaluations if they were concerned that their condition was deteriorating. Follow-up evaluations consisted of an update of clinical and medical status, including notation of any treatment contacts or use of medication. At each visit the patient completed the Beck Depression Inventory, and the evaluator rated the patient's clinical status with the Hamilton depression scale and the GAS. The evaluator also inquired whether the patient had experienced any wors-

ening of his or her condition during the interval since the most recent assessment (i.e., a 1- to 3-month interval) that might not be reflected by the current status. A checklist summarizing the *DSM-III-R* criteria for major depression was completed by the independent evaluator at each visit to describe the patient's syndromal status at the worst point during the follow-up interval.

Patients were considered to have relapsed if at any time they 1) met the *DSM-III-R* criteria for major depression for a minimum of 2 weeks and 2) had a Hamilton depression score of 15 or more. All relapsed patients were retreated by our program. We also recorded when patients reentered treatment for other reasons and when they met the less restrictive criteria for partial relapse (minor or intermittent depression according to the RDC), experienced a transient worsening that had lessened by the time of assessment, and/or had Hamilton depression scores that deviated from the response range (greater than 10 but less than 15).

The first planned step of the data analysis involved dividing the study group into subgroups who either relapsed or remained well, as we have described. Second, the pretreatment demographic and clinical characteristics of these groups were compared using Fisher's exact probability test, chi-square test, or Student's *t* test, as appropriate for categorical or continuous variables. Given the exploratory nature of these analyses, we used two-tailed tests but did not correct for the "inflation" of the alpha rejection factor that is associated with performing such multiple comparisons. Third, we compared the patients who relapsed and the patients who remained well with respect to end-of-treatment symptom status and speed of response to acute treatment (i.e., number of weeks from the onset of therapy until the patient first met the response criteria). Finally, the risk of relapse during the 12-month follow-up for the recovered and partially recovered groups was compared using survival analysis of life table data and tested with Wilcoxon's chi-square statistic.

RESULTS

Forty-nine of the 50 patients who were enrolled completed all scheduled visits during the 1-year follow-up program; the remaining patient dropped out after 6 months. A total of 16 patients (32%) relapsed. The patients who relapsed did not differ from those who remained well on most demographic variables, including age, sex, age at onset of the first episode of depression, and mean number of previous depressive episodes (table 1). However, patients who relapsed were significantly less likely to be married: 31% (*N*=5) of them were married, compared to 65% (*N*=22) of the patients who did not relapse ($\chi^2=7.32$, *df*=2, *p*<0.05). There was a trend for those who relapsed to have had at least one previous episode of major depression (table 1). The relapsers also had significantly higher pretreatment scores on the Hamilton depression scale, the Beck Depression Inventory, and the Dysfunctional Attitude

Scale, although the between-group difference on the GAS did not reach statistical significance (table 1).

At the end of treatment, patients who subsequently relapsed continued to have significantly higher residual scores on the Hamilton depression scale and the Dysfunctional Attitude Scale (table 1). A similar trend in posttreatment scores was apparent on both the GAS and the Beck Depression Inventory, although neither finding reached significance after adjustments for heterogeneity of variance (for both, adjusted *p*=0.06) (table 1). Patients who subsequently relapsed also showed a significantly longer time to response during acute treatment, with an average of more than 3 weeks of additional therapy received before response criteria were fulfilled (table 1). Finally, only 9% (*N*=2) of the patients who met the criteria for full recovery by the time of treatment termination subsequently relapsed, compared to 52% (*N*=14) of the partially recovered patients (Wilcoxon $\chi^2=10.63$, *df*=1, *p*=0.004) (figure 1).

Because of the association between a number of patient characteristics and risk of subsequent relapse, the survival analysis was repeated using the Cox proportional hazards regression model (21), which allows the relationship of the time elapsed to a categorical endpoint, such as relapse, to be modeled with respect to the influence of both independent variables and covariates. Patient characteristics often are entered as covariates, and covariates may be either continuous or categorical variables. The hazard function represents the probability of the outcome in question (for instance, relapse) per unit of elapsed time in follow-up. With the Cox model, the influence of a series of variables on the hazard function can be determined, both singly and in combination, using a stepwise multivariate analysis. As with any multivariate procedure, it is important to have a sufficient number of subjects for each variable studied. With 50 subjects, we chose five covariates of particular interest: time to response, marital status (married versus other), history of past episodes (yes versus no), posttreatment Hamilton depression scale score, and posttreatment Dysfunctional Attitude Scale score. Using the proportional hazards regression model, we tested each of the five covariates independently after adjusting for the other four effects. This method was used because of the unbalanced nature of the data. Both time to response ($\chi^2=6.18$, *df*=1, *p*=0.01) and marital status ($\chi^2=4.4$, *df*=1, *p*=0.03) were statistically related to the hazards function and contributed additively to prediction of outcome. Posttreatment score on the Dysfunctional Attitude Scale was a marginally significant covariate when other effects were controlled. Neither a history of past episodes ($\chi^2=2.34$, *df*=1, *p*=0.13) nor pretreatment Hamilton depression scale score ($\chi^2=1.55$, *df*=1, *p*=0.21) was statistically significant after accounting for the other effects ($\chi^2=3.04$, *df*=1, *p*=0.08). When a model using time to response, marital status, and posttreatment score on the Dysfunctional Attitude Scale was studied, the analysis yielded a significant relation to risk of relapse (global $\chi^2=12.85$, *df*=3, *p*=0.005).

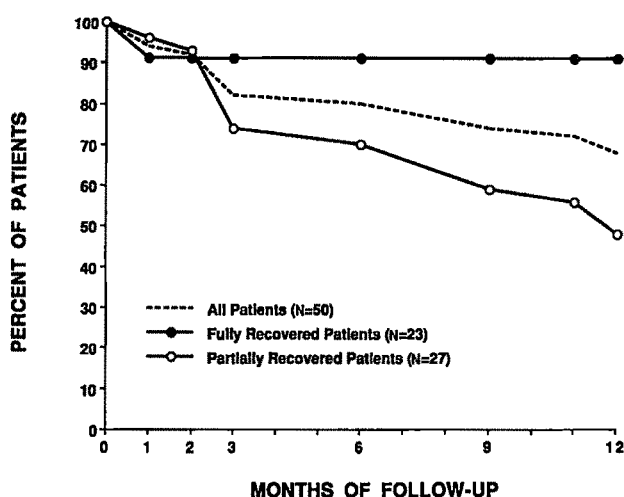
During the 1-year follow-up, only five patients who

TABLE 1. Characteristics of a Group of 50 Depressed Patients Who Received Cognitive Behavior Therapy for Depression and the Subgroups Who Had Relapsed or Maintained Improvement at 1-Year Follow-Up

Characteristic	Total Group (N=50)	Patients Who Relapsed (N=16)	Patients Who Maintained Improvement (N=34)	Analysis
Age (years)				t=0.43, df=48, n.s.
Mean	37.3	38.1	36.9	
SD	9.0	8.1	9.5	
Sex				p=0.33, Fisher's exact test
Male				
N	15	3	12	
%	30	19	35	
Female				
N	35	13	22	
%	70	81	65	
Education (years)				t=0.69, df=48, n.s.
Mean	14.5	14.7	14.4	
SD	2.5	2.5	2.5	
Duration of episode (weeks)				t=0.85, df=48, n.s.
Mean	42.3	43.1	41.9	
SD	21.6	23.1	21.2	
Age at onset (years)				t=0.15, df=48, n.s.
Mean	31.0	31.4	30.9	
SD	10.8	10.6	11.0	
Occurrence of previous episodes				$\chi^2=3.31$, df=1, p=0.07
Yes				
N	25	11	14	
%	50	69	41	
No				
N	25	5	20	
%	50	31	59	
Number of previous episodes				t=0.18, df=48, n.s.
Mean	1.4	1.4	1.5	
SD	2.0	1.4	2.2	
Pretreatment characteristics				
Hamilton depression scale score				t=2.33, df=48, p<0.05
Mean	21.6	22.8	20.2	
SD	3.8	3.2	3.8	
Beck Depression Inventory score				t=1.98, df=48, p<0.05
Mean	27.2	30.1	25.8	
SD	7.6	6.4	7.8	
GAS score				t=1.97, df=48, p<0.05
Mean	53.2	50.3	54.5	
SD	7.4	7.0	7.2	
Dysfunctional Attitude Scale score ^a				t=1.94, df=43, n.s.
Mean	140.1	153.7	133.3	
SD	34.3	28.0	35.5	
Posttreatment characteristics				
Hamilton depression scale score				t=2.28, df=20.5, ^b p<0.05
Mean	3.2	4.9	2.4	
SD	3.2	4.0	2.5	
Beck Depression Inventory score				t=1.99, df=20.1, ^b n.s.
Mean	5.4	8.3	4.1	
SD	6.0	7.7	4.6	
GAS score				t=1.97, df=20.3, ^b n.s.
Mean	87.9	83.4	90.0	
SD	9.7	12.4	7.5	
Dysfunctional Attitude Scale score ^c				t=2.68, df=46, p<0.05
Mean	112.0	132.1	102.8	
SD	37.4	30.1	37.2	
Weeks to response				t=2.60, df=48, p<0.05
Mean	10.6	12.9	9.5	
SD	4.7	4.1	4.5	
Full versus partial recovery				$\chi^2=8.61$, df=1, p<0.01
Full recovery				
N	23	2	21	
%	46	12	62	
Partial recovery				
N	27	14	13	
%	54	88	38	

^aN=45.^bAdjusted for unequal variance.^cN=48.

FIGURE 1. Survival Curves of Time to Relapse After Termination of Cognitive Behavior Therapy for Depressed Patients^a



^aSignificant difference between fully recovered and partially recovered patients (Wilcoxon $\chi^2=10.63$, $df=1$, $p=0.004$).

did not meet the full criteria for relapse met any of the "softer" criteria for relapse (transient or minor depression, return to treatment, and/or Hamilton depression scale score higher than 10 but lower than 15). Reassignment of these patients to the group of relapsed patients did not alter any of the findings of significance.

DISCUSSION

The 32% rate of relapse into depression observed during the 1-year prospective follow-up protocol is generally consistent with the rates reported by other investigators studying outcome after cognitive behavior therapy (3–6). Unlike several of the earlier follow-up studies (3, 4), however, our protocol included certain methodological refinements, such as use of regularly scheduled and standardized independent assessments, operationalized diagnostic criteria to define relapse, and maximal control over reentry into treatment. These features increase confidence in the ascertainment of cases of relapse. Of course, in the absence of appropriate control groups, we are not able to comment on whether acute cognitive behavior therapy actually lowered the inherent risk of relapse for our patients, particularly compared to patients treated with antidepressant medications or other forms of psychotherapy.

Patients who subsequently relapsed were more likely to be unmarried, tended to be suffering from a recurrent episode of depression, and reported higher levels of depressive symptoms and dysfunctional attitudes when they entered the study. They also ended acute treatment with higher levels of residual symptoms and had a slower response during therapy. Furthermore, the relatively straightforward division of the study group into recovered and partially recovered subgroups yielded a

highly significant association with subsequent outcome, with the partially recovered patients having a more than five times greater risk of depressive relapse than the fully recovered patients. Thus, although the findings of statistical significance may have been inflated somewhat by the exploratory nature of the univariate analyses, the results are consistent with those of earlier studies (3–9) and, with respect to the risk of relapse in partially recovered patients, they are both clinically relevant and robust.

Cognitive behavior therapy differs from other psychotherapies developed for depression, in part, because the final sessions of therapy are devoted to preparing for the possibility of relapse (1, 22). Patients treated with cognitive behavior therapy are encouraged to learn to identify or anticipate situations or problems that may increase their risk of relapse, and they spend time in therapy addressing these issues. Further, patients are asked to assume progressively more responsibility for independent application of therapeutic techniques during the final weeks of treatment, so that they can continue to use cognitive behavior therapy self-help methods long after termination of treatment (1, 22). It is of interest, therefore, that the relapse rates of the recovered and partially recovered subgroups did not begin to diverge until about 3 months after the end of therapy. Indeed, only about 10% of the patients in both the fully and the partially recovered subgroups relapsed during the first 2 months of follow-up. Thus, the difference in relapse rates between these subgroups does not appear to have been due to a rapid deterioration of clinical status immediately after withdrawal of the therapist's support and input. Rather, we suggest that many partially recovered patients struggle for at least several months to continue to apply techniques learned in therapy to cope with residual symptoms or psychosocial problems before ultimately relapsing into an episode of major depression.

During pharmacotherapy of unipolar major depression, a period of at least 4 months of continuation therapy after an acute response to drug treatment is now routinely recommended in order to reduce the risk of relapse (8, 9). For acutely depressed patients who respond rapidly to an antidepressant medication of first choice, the minimum course of treatment is thus about 5 or 6 months long. By contrast, an extended course of maintenance pharmacotherapy is typically recommended for patients who have experienced multiple episodes of depression or for those who manifest residual depressive symptoms despite continuation pharmacotherapy (8, 9). From this perspective, the 4-month course of cognitive behavior treatment provided in the Psychobiology of Recovery in Depression project protocol approximates the length of time usually spent in both the acute and continuation phases of pharmacotherapy for acute, uncomplicated major depression. Therefore, it is interesting that the 52% relapse rate documented in our partially recovered patients is so similar to the 40%–60% risk of relapse observed when medication responders do not re-

ceive an adequate period of continuation pharmacotherapy (8, 9).

Other investigators have documented the significance of a slow response to initial treatment or higher levels of residual symptoms in predicting relapse of patients with unipolar depression (3, 5, 6, 20, 23, 24). The relation between residual symptoms and recurrence of depression appears to be attenuated or even eliminated when a longer period of continuation pharmacotherapy is provided (25). We are not yet able to ascertain whether our partially recovered and fully recovered patients differed only with respect to general prognostic factors (higher levels of residual symptoms, slower response to initial therapy, greater past history of depression, and/or lower levels of social support) or whether they also differed on variables that reflect the process and course of therapy (the strength of the therapeutic alliance, compliance with homework assignments, and/or the technical quality of the therapist's interventions). It also may be useful to try to differentiate between the partially recovered patients who relapsed and those who did not. Nevertheless, we consider the 52% relapse rate of the partially recovered patients to be a clear indication for the need to develop, implement, and test alternative methods for treating such patients. Further, it seems likely that if patients with so-called "double depression" had been enrolled in our study, the relapse rate would have been even higher (20).

We therefore recommend that patients who do not fully recover from a depressive episode after time-limited psychotherapy should be considered for either more extended therapy or for other treatment modalities. One such revised treatment plan would consist of prolonging the course of weekly cognitive behavior therapy until the patient meets criteria for recovery. For some patients, this recommendation could entail a 6-, 9-, or even 12-month course of therapy. Alternatively, an ongoing but less intensive approach of maintenance psychotherapy might prove useful. In our clinical practices, we sometimes provide a period of several months of biweekly visits, followed by a number of monthly sessions, to patients considered to be at high risk for relapse. With respect to the efficacy of maintenance psychotherapy, Frank et al. (25) recently demonstrated the value of monthly sessions of interpersonal psychotherapy (relative to a placebo-treatment control group) in a study of patients with highly recurrent forms of unipolar depression.

On the other hand, it might be suggested that patients who manifest residual symptoms after short-term cognitive behavior therapy have more virulent or "endogenomorphic" forms of depression which, perhaps, would be treated more appropriately by pharmacotherapy than by additional sessions of psychotherapy. Beyond the work of Elkin et al. (26) and our own previous report linking greater initial severity of depression with somewhat poorer absolute response to cognitive behavior therapy (11), we are not aware of strong empirical support for this hypothesis. Moreover, many of the partially recovered patients at risk for relapse in our study

ended treatment with Hamilton depression scale scores in the 3- to 8-point range, a level of symptoms that would not normally justify the initiation of pharmacological treatment.

It also seems clear that not all patients treated with cognitive behavior therapy would benefit from more extensive treatment. For example, the low (9%) risk of relapse among the fully recovered patients suggests that a great majority of patients who achieve such favorable acute outcomes during time-limited therapy continue to do well without additional treatment, at least during the first year after termination of therapy. Perhaps the low risk of relapse among fully recovered patients in the Psychobiology of Recovery in Depression study might explain why Baker and Wilson (27) found no evidence of protection from relapse when additional "booster" cognitive behavior therapy sessions were provided, unselectively, to a small sample of therapy responders.

In summary, a series of 50 patients who improved during a time-limited course of cognitive behavior therapy were enrolled in a systematic, longitudinal, 1-year follow-up protocol. A number of clinical correlates of subsequent relapse were identified, and parallels were drawn between the risks of depressive relapse after time-limited psychotherapy and those after a short-term course of antidepressant pharmacotherapy. As in pharmacotherapy of unipolar depression, we suggest that longer-term models of continuation and/or maintenance psychotherapy may be necessary for selected patients at high risk for relapse or recurrence.

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Protective Effects of Imipramine Maintenance Treatment in Panic Disorder With Agoraphobia

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Objective: This study was designed to assess and compare the differential relapse rates of patients with panic disorder and agoraphobia after discontinuation of acute treatment (6 months) or acute plus maintenance treatment (18 months) with imipramine. **Method:** Sixteen patients with panic disorder and agoraphobia who had shown marked and stable response to 6 months of acute imipramine treatment and a comparable group of 14 patients who had been in remission during an additional year of half-dose imipramine maintenance treatment entered a 3-month, double-blind discontinuation study followed by a 3-month drug-free period. Assessments of the patients were made according to operationalized response/relapse criteria, and plasma drug concentrations were monitored. **Results:** Survival analysis revealed significantly different cumulative probabilities of continued response 6 months after discontinuation of imipramine treatment between the patients who had received only acute treatment and those who had received acute and maintenance treatment. **Conclusions:** The results support the hypothesis that successful imipramine maintenance treatment of patients with panic and agoraphobia can have protective effects against relapse, at least in the first 6 months after the maintenance treatment period.

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Patients with panic disorder and agoraphobia, like those suffering from obsessive-compulsive disorder (1) and unipolar depression (2), are likely to relapse when pharmacotherapy with antidepressants is discontinued (3-6). Recently, we reported (7) that approximately 75% of patients with panic disorder and agoraphobia who had shown marked and stable response to 6 months of acute treatment with imipramine relapsed within 6 months of discontinuing the drug. In contrast, none of the patients from a similarly treated sample who had responded to imipramine and who had received maintenance treatment with the drug for 12 additional months (at one-half the dose they received during acute treatment) relapsed or had sustained worsening of panic or phobic symptoms throughout the 1-year maintenance period. In the present study we explored the potential protective effects of imipramine maintenance treatment against relapse in these two samples by comparing the cumulative relapse rates 6

months after discontinuation of acute imipramine treatment and 6 months after discontinuation of acute plus maintenance imipramine treatment. Studies of monoamine oxidase inhibitors (MAOIs) in mixed anxiety-phobic diagnostic groups (8, 9) have suggested that although there is still substantial relapse, it is less among patients who discontinue drug treatment after 1 year than among those treated for 6 months or less.

METHOD

The experimental groups of the present study were derived from the consecutive samples previously studied (7). One group consisted of 16 patients who entered the discontinuation protocol immediately after acute imipramine treatment (the acute group). The other consisted of 14 patients (of the 19 who participated in the maintenance study) who entered the discontinuation protocol upon successful completion of 1 year of imipramine maintenance therapy at one-half the dose received during their acute treatment (the delayed group). The method of subject selection, the acute and maintenance treatments used, and the assessments of the patients have been previously described in detail (7, 10, 11).

Briefly, all of the subjects were outpatients meeting the DSM-III-R criteria for panic disorder with agoraphobia who had shown good and stable response to an open imipramine protocol at a dose of 2.25 mg/kg per

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day over an initial 24-week acute treatment period. At week 8 of their acute treatment, patients were also given a behavioral rationale for self-directed exposure to phobic situations and a programmed practice manual to read and apply to their situations (12). No additional sessions for monitoring self-directed practice of exposure were offered. Thus, the behavioral therapy input was limited to providing all patients with the same information regarding exposure. Patients were assessed after 16 and 24 weeks of acute treatment, and the first consecutive 19 patients who met operationalized criteria for responder status at both assessments participated in the prospective 1-year open maintenance study at one-half the imipramine dose received during acute treatment. No additional treatment for agoraphobia or panic was provided during the maintenance phase, which was successfully completed by 14 patients without a single relapse. (The noncompleters did not differ significantly from the 14 completers on demographic or clinical variables before acute treatment and were responders up to the point of dropping out of the maintenance study.) These 14 patients formed the delayed experimental group of the present study. The next 16 consecutive patients who met the operationalized criteria for responder status consented to participate in the discontinuation protocol immediately after their 24-week acute treatment assessment (the acute group).

Because the present study group of 30 patients was derived from two groups of responders who had been consecutively rather than randomly assigned to maintenance and acute treatment groups, we performed 2x2 Group by Time (pretreatment and end of active treatment) analyses of variance (ANOVA) on the seven major outcome measures, described below, to ensure that the groups were comparable in initial severity of illness and response to acute treatment. As expected, there were significant time effects on all measures but no main effects of group, which would have indicated different overall levels of severity. It is also noteworthy that, with one exception, there were no Group by Time interactions, indicating that the groups improved equally during acute treatment. The exception was in clinician-rated severity of panic and reflected the slightly higher pretreatment ratings of the acute group: the pretreatment and end-of-treatment mean ratings were 2.6 (SD=0.7) and 0.2 (SD=0.4), respectively, for the acute group and 2.1 (SD=0.3) and 0.4 (SD=0.5), respectively, for the maintenance group ($F=5.03$, $df=1, 25$, $p=0.03$).

The mean age of the total study group was 34.2 years (SD=8.0); their mean number of years of education was 13.9 (SD=2.1). Sixty-seven percent ($N=20$) of the patients were female, 60% ($N=18$) were married, and 70% ($N=21$) were currently employed. The average age at onset of panic disorder was 27.9 years (SD=6.7), and the average duration of illness was 6.4 years (SD=6.3). There were no concurrent diagnoses of major depression or substance abuse; however, 27% ($N=8$) of the patients had histories of past major depression, and 17% ($N=5$) had histories of past substance abuse. Patients in the delayed group

were significantly older (mean age=38.1 years, SD=8.0) than those in the acute group (mean=30.7 years, SD=6.2) ($t=2.86$, $df=28$, $p=0.01$), and they had a longer duration of illness (mean=9.1 years, SD=7.9) than the acute group (mean=4.1 years, SD=3.3) ($t=2.30$, $df=28$, $p=0.03$). The stable imipramine dose received during acute treatment was not significantly different for the two experimental groups and averaged 2.1 mg/kg per day (SD=0.3) (mean=145.8 mg/day, SD=35.4) for the group as a whole.

The design of the present study consisted of a 3-month double-blind drug discontinuation phase followed by a 3-month drug-free follow-up period. The study was initiated (month 0) by converting from open prescription of imipramine to double-blind administration of four identical-looking tablets containing either placebo or 10, 25, 50, or 75 mg of imipramine hydrochloride. The drug condition for each patient was known only by the hospital pharmacist, who followed a procedure to ensure equal distribution of placebo ($N=8$) and imipramine ($N=8$) in the acute group and an assignment ratio of three patients receiving placebo ($N=10$) to one patient receiving imipramine ($N=4$) in the delayed group. Those assigned to imipramine received the same dose, or extremely close to it, for 3 months. Discontinuation was achieved by 25% decrements each week, so that a zero imipramine dose (four placebo tablets) was reached on the 22nd day of randomization. Patients were instructed, indeed encouraged, to contact us for any psychiatric or psychological problems that they might have, with the understanding that they would be seen immediately and appropriate clinical action would be taken. Otherwise, they were assessed on a monthly basis for 3 months, when the drug code was broken. A concerted effort was made to follow patients in the placebo condition who had not relapsed for an additional 3-month drug-free period.

The same battery of tests that had been used to determine all patients' response status during acute treatment and the delayed group's status during maintenance treatment (7) was used in the present study. Responders were operationally defined as those who 1) showed a simultaneous reduction of 50% or more from pretreatment values on six or all seven of the response measures or 2) had scores that signified minimal or absent symptoms, as follows: score of 2 or less on the Global Assessment of Severity Scale, score of 2 or less on the Self-Rating Scale of Severity of Phobias, score of 10 or less on the Agoraphobia subscale of the Fear Questionnaire, score of 2 or less on the Phobic Anxiety and Avoidance Scale, score of 2 or less on the Behavioral Assessment Test, panic severity rating of 2 or less by the patient, and panic severity rating of 1 or less by the clinician. For this study relapse was defined a priori as meeting no more than four of these criteria and requiring or requesting treatment for panic or agoraphobia. (Detailed descriptions of the seven dependent measures are given elsewhere [7, 10, 11].)

At each assessment blood samples were drawn 12 hours after the preceding dose and collected into plasticizer-free Vacutainers. The samples were promptly

TABLE 1. Cumulative Relapse Rates Among Patients With Panic Disorder and Agoraphobia Who Received Placebo After Discontinuation of Imipramine Treatment

Time Since Discontinuation	Relapsers in Acute Group (N=8) ^a		Relapsers in Delayed Group (N=10) ^b	
	N	%	N	%
3 months	3	38	1	10
6 months				
Observed relapse rate ^c	5	83	2	25
Relapse rate if the four patients lost to follow-up are counted as responders	5	62	2	20
Relapse rate if the four patients lost to follow-up are counted as relapsers	7	88	4	40

^aPatients who had received 6 months of acute imipramine treatment only.

^bPatients who had received 6 months of acute plus 1 year of maintenance imipramine treatment.

^cN=6 for the acute group; N=8 for the delayed group.

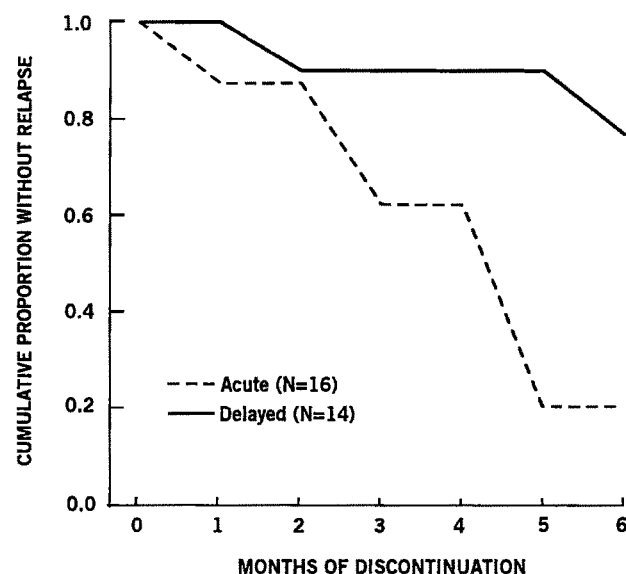
centrifuged and stored at -20°C for later determination of drug concentrations by a modified high-performance liquid-chromatography technique (10, 13, 14).

RESULTS

All 30 subjects were responders at the time they were randomly assigned to the study groups. As a further check on randomization, ANOVAs with the two groups (acute, delayed) and two conditions (imipramine, placebo) were performed on the seven dependent measures at month 0. No significant main effects of condition or interaction effects were found, although, as could be expected from the consolidation of improvement previously reported during the 1-year half-dose maintenance protocol (7), statistically significant group main effects emerged for scores on the Self-Rating Scale of Severity of Phobias and the Agoraphobia subscale of the Fear Questionnaire; the delayed group had slightly lower scores on these two measures. As expected, the dose of imipramine was significantly different for the acute and delayed groups (mean=2.04 mg/kg per day, SD=0.23, and mean=1.07 mg/kg per day, SD=0.10, respectively; $t=14.38$, $df=28$, $p<0.01$).

Analysis of monthly plasma levels revealed tricyclic concentrations of 0 ng/ml in all patients assigned to placebo. Repeated measures ANOVAs on plasma data for month 0 through month 3 of the patients assigned to the imipramine continuation condition did not reveal significant effects of time on total tricyclic levels or plasma level/dose ratios, indicating generally good compliance with the experimental conditions. The average total tricyclic levels, according to all available plasma data from patients in the imipramine condition, were 158 ng/ml (SD=57.0) and 55 ng/ml (SD=26.6) for the acute and delayed groups, respectively.

With one exception, none of the patients assigned to

FIGURE 1. Six-Month Survival Curves of Patients With Panic Disorder and Agoraphobia After Discontinuation of 6 Months of Acute Imipramine Treatment (Acute Group) or 6 Months of Acute Plus 1 Year of Maintenance Imipramine Treatment (Delayed Group)

imipramine in the double-blind phase of the study relapsed. The exception occurred in the acute group during the second month of the protocol, at the time of a patient's increased distress due to exacerbation of her husband's medical condition. The drug code was broken and the patient continued to take study medications for another month, when she was again a responder.

Table 1 shows relapse rates within 6 months of imipramine discontinuation for the acute and delayed groups assigned to placebo. Because four of the 14 survivors from the double-blind placebo phase were lost to follow-up in the subsequent 3-month drug-free period, we used three scenarios to estimate 6-month cumulative relapse rates. As can be seen in table 1, the frequency of relapse in the acute group consistently exceeded that of the delayed group by a ratio of 2 or 3 to 1. For statistical analysis of the data we used the Kaplan-Meier product limit method to estimate and the Mantel-Cox method to compare the 6-month survival curves in the acute and delayed placebo groups (15). The results are illustrated in figure 1 and show that the cumulative probability of continued response 6 months after discontinuation of imipramine was 0.21 in the acute group (mean survival of 3 months) and 0.77 in the delayed group (mean survival of 5.2 months). Comparison of the observed test statistic, $\chi^2=4.06$, with a chi-squared distribution value of 3.84, with 1 degree of freedom ($p=0.05$), leads to rejection of the null hypothesis that the two curves are the same.

Of the five observed relapses in the acute placebo group, one occurred within 1 month of discontinuation, two during the third month of the discontinuation study, and two during the fifth month of the study. One of the patients in the delayed group relapsed during the third month and the other relapsed during

TABLE 2. Panic and Phobia Scores of Seven Patients With Panic Disorder and Agoraphobia Before Acute Imipramine Treatment, Before the Drug Discontinuation Phase of the Study (Month 0), and at Relapse^a

Measure (range of possible scores)	Before Treatment		Month 0		Relapse	
	Mean	SD	Mean	SD	Mean	SD
Global Assessment of Severity Scale (1–5)	3.7	0.5	1.3	0.5	2.7	0.5
Self-Rating Scale of Severity of Phobias (0–8)	6.4	0.8	0.7	0.8	4.6	1.4
Phobic Anxiety and Avoidance Scale (0–8)	6.8	1.1	1.7	1.2	4.2	1.9
Agoraphobia subscale of the Fear Questionnaire (0–40)	24.7	7.1	3.3	3.0	12.3	6.0
Behavioral Assessment Test (0–8)	4.2	2.0	0.3	0.4	— ^b	—
Panic severity						
Patient rating (0–8)	5.6	1.4	0.9	1.9	5.6	1.5
Clinician rating (0–4)	2.4	0.5	0.1	0.4	2.4	0.5

^aAll differences between scores at month 0 and at relapse were significant at $p < 0.05$ according to analysis of variance.

^bThere were no data for five of the seven patients.

the sixth month of the study. The relapse of these seven patients is characterized in table 2. It can be seen that both phobic and panic symptoms became substantially worse and that ratings of panic severity returned to pre-treatment levels. The pattern of change was the same in individual patients, and all of them were having panic attacks at the time of relapse. The patients who relapsed clinically required and personally requested resumption of imipramine treatment. None of them met diagnostic criteria for major depression at the time of relapse.

DISCUSSION

Panic disorder with agoraphobia is a prevalent syndrome (16), and imipramine is the standard nonbenzodiazepine pharmacotherapy, yielding approximately 75% marked response rates when it is the sole or main treatment (11, 17). Reported relapse rates after discontinuation of imipramine (or MAOIs) vary from 17.5% to 100%, partly reflecting varying definitions of relapse, which are often unspecified, and partly reflecting varying dosages and duration of treatment or degrees of improvement/response before drug discontinuation (3–5). The present study offers clear methodological advantages in this respect. The subjects consisted of two consecutive groups of homogeneously selected and uniformly treated patients with panic disorder and agoraphobia who had shown marked and stable response to 6 months of acute treatment with imipramine. Furthermore, operationalized criteria for response and relapse were uniformly applied, discontinuation of imipramine for the first 3 months of the study was double-blind, and the use of plasma drug level determinations verified the integrity of experimental drug conditions.

The salient difference between the otherwise compa-

rable acute and delayed groups—namely, the additional successful maintenance therapy received by the latter—was the experimental variable of interest in our investigation of the potential effects of maintenance therapy as protection against relapse. Thus, although determination of the exact magnitude of the problem of relapse after discontinuation of imipramine treatment should await large-scale, double-blind studies over longer periods of time, the differential relapse rates of the acute and delayed groups in the present study support the hypothesis that 1 year of successful imipramine maintenance treatment at one-half the dose received during acute treatment can have protective effects against relapse, at least in the first 6 months after the maintenance treatment period. Whether this protective effect continues for longer periods of time and whether longer durations of imipramine maintenance therapy would have greater and more enduring protective effects in patients with panic disorder and agoraphobia are empirical questions worthy of study.

Because none of the patients in the delayed group had received other specific treatments for panic/agoraphobia during maintenance therapy, and in light of the high relapse rate in the acute group, we have suggested that the stability of gains during the open maintenance treatment period was due primarily, if not specifically, to continued exposure to imipramine (7). Whether the reduced imipramine dose during maintenance treatment contributed, significantly and independently of duration of remission, to the protective effects against relapse upon discontinuation of imipramine remains an interesting and important question to be elucidated. It is unlikely that the mechanisms involved in the differential relapse rates were related to withdrawal, since no patient reported difficulty or untoward effects in the first 3 weeks of gradual discontinuation of imipramine, and only one of the relapses occurred during the first month of the study. It is possible, however, that excessive down-regulation of putative β -adrenergic and serotonergic receptors was moderated through the administration of the half-doses (as compared to full doses) of imipramine during maintenance treatment. There is clear experimental evidence that imipramine, in a dose-dependent fashion, reduces the density of β -adrenergic receptors in the cerebral cortex (18).

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The Latent Structure of Anxiety Symptoms in Anxiety Disorders

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Objective: Research in the psychopathology of panic and anxiety disorders, particularly agoraphobia, suggests that fear of fear may be the basis of these conditions. However, there is little empirical research on the definition and validity of the concept of fear of fear in a clinical study group. The authors' aims are 1) to determine empirically if particular associations between symptoms and beliefs exist in a group of patients with anxiety disorders and what underlying dimensions of perceived threat they represent and 2) to assess the relative importance of these associations in agoraphobia with panic attacks, panic disorder, social phobia, and generalized anxiety disorder. **Method:** In an anxiety disorders treatment unit, 390 outpatients with anxiety disorders diagnosed according to DSM-III criteria completed the Anxiety Symptoms and Beliefs Scale. **Results:** A principal components analysis of the patients' ratings on the Anxiety Symptoms and Beliefs Scale produced a four-factor solution in which specific sets of anxiety symptoms loaded with specific beliefs. These four factors were interpreted as respiratory symptoms, vestibular symptoms, autonomic arousal, and psychological threat. Respiratory and vestibular symptoms were more associated with panic disorder diagnoses than with social phobia and generalized anxiety disorder diagnoses. **Conclusions:** These findings support a conception of fear of fear in anxiety disorders as fearful beliefs concerning the experience of anxiety symptoms. Associations between symptoms and fear of fear are present across anxiety disorders but are most pronounced in agoraphobia with panic attacks.

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By making agoraphobia secondary to a diagnosis of panic disorder, *DSM-III-R* elevated the status of panic attacks in clinical presentation. An important change made to the new diagnostic criteria for panic disorder has been the optional waiving of the frequency criterion of four panic attacks in a 4-week period. The alternative criterion requires that "one or more attacks have been followed by a period of at least a month of persistent fear of having another attack." This criterion recognizes the importance of fear of panic attacks, or fear of fear.

The concept of fear of fear in agoraphobia and panic disorder is not new (1-4). Goldstein and Chambless (4) conceived the core of agoraphobia as the fear of harmful consequences of experiencing anxiety symptoms. Subsequently, Chambless et al. (5) developed companion

measures of fear of fear called the Body Sensations Questionnaire and the Agoraphobic Cognitions Questionnaire. More recently, Reiss and McNally (6) proposed a formulation of fear of fear as the dual-component processes of anxiety expectancy and anxiety sensitivity. Anxiety expectancy is the expression of the learned association between anxiety symptoms and fear. Anxiety sensitivity is the belief that anxiety and anxiety symptoms are dangerous. This belief was seen as underlying anxiety in general. Thus, associations of specific symptoms and beliefs were not thought to be important in the presentation of fear of fear; rather, fear of harmful consequences of any type of anxiety symptom or anxiety in general was seen to underlie anxiety.

Beck et al. (7) suggested that particular feared outcomes maintain particular anxiety disorders. For example, perceived threats to physical and mental health are seen as central to agoraphobia, whereas perceived threats to social acceptability and performance are associated with social phobia. Studies to date have examined the construct of fear of fear either by measuring symptoms and beliefs separately (5) or by arbitrarily attaching symptoms to particular consequences (8). Further, there has not been any empirical evidence supporting the validity of associations between symptoms and beliefs as expressions of fear of fear.

The aims of this study were 1) to determine empirically if particular associations between symptoms and beliefs

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TABLE 1. Characteristics of 390 Patients With Anxiety Disorders

Diagnostic Group	Sex				Age (years)		Age at Onset of Disorder (years)	
	Men		Women		Mean	SD	Mean	SD
	N	%	N	%				
Panic disorder (N=53)	16	30	37	70	33.79	7.94	30.85	9.66
Generalized anxiety disorder (N=37)	12	32	25	68	37.43	10.02	29.80	10.75
Agoraphobia with panic (N=246)	62	25	184	75	37.72	11.54	30.15	10.58
Social phobia (N=54)	22	41	32	59	31.87	9.04	25.45	7.68
Total (N=390)	112	29	278	71	36.37	10.86	29.76	7.68

exist in a group of patients with anxiety disorders and what underlying dimensions of perceived threat they represent and 2) to assess the relative importance of these associations in agoraphobia with panic attacks, panic disorder, social phobia, and generalized anxiety disorder.

METHOD

Subjects

Of 529 patients who came sequentially to an anxiety disorders clinic between 1981 and 1987 for assessment and treatment in an intensive group cognitive-behavioral program, 390 who met *DSM-III* criteria for one of four anxiety disorder diagnoses were selected for study. Fifty-three of these patients had panic disorder, 246 had agoraphobia with panic attacks, 54 had social phobia, and 37 patients had generalized anxiety disorder. The patients who had the *DSM-III* diagnosis of agoraphobia with panic attacks also met *DSM-III-R* criteria for panic disorder with agoraphobia. Table 1 presents the characteristics of the study group. The sex ratio did not differ among groups ($\chi^2=4.21$, $df=3$, n.s.), although women were in the majority in each group (table 1). The patients with agoraphobia with panic attacks and those with generalized anxiety disorder were significantly older than the patients with social phobia ($F=5.55$, $df=3$, 384, $p=0.001$). The mean age at onset was not significantly different across groups ($F=2.24$, $df=3$, 328, n.s.).

Measures

The Anxiety Symptoms and Beliefs Scale was adapted from the Agoraphobia Survey Schedule (9). For example, the fear of starting to scream was excluded because in our clinical experience this is rarely reported as a belief. The instrument assesses the intensity on a 5-point scale of 16 symptoms of extreme anxiety and five beliefs (fears) concerning the consequences of panic. The symptoms include those prescribed by *DSM-III* and *DSM-III-R* as constituting a panic attack.

Procedure

The procedure for assessment and diagnosis has been fully described elsewhere (10). After referral, patients

TABLE 2. Intercorrelations Between Rotated Factors for 335 Patients With Anxiety Disorders

Factor	Correlation (r)		
	Factor 1	Factor 2	Factor 3
Factor 1 (vestibular symptoms)			
Factor 2 (respiratory symptoms)	0.30		
Factor 3 (psychological threat)	0.33	0.24	
Factor 4 (autonomic arousal)	0.44	0.55	0.37

completed the Anxiety Symptoms and Beliefs Scale. Subsequently, the patients participated in a structured interview with a staff psychiatrist or clinical psychologist skilled in assessment and diagnosis of anxiety disorders using *DSM-III* criteria. The interview lasted about 1.5 hours during which a life history was taken, self-report forms were reviewed with the patient, and clinical rating scales were administered. The case history was then presented to a meeting of all clinical staff and a diagnosis was determined. All patients provided informed consent to their participation in the study.

RESULTS

To assess the underlying association between the physical anxiety symptoms and the belief items a principal components analysis was performed on the patients' ratings of the 21 items of the Anxiety Symptoms and Beliefs Scale. The number of patients included in the analysis was 335 after listwise deletion of missing values was applied. The number of factors was determined by applying the criterion of an eigenvalue greater than 1.0. Further inspection of eigenvalues revealed a substantial break in the percentage of variance between the fourth and fifth components and a gradual decline in variance thereafter. The four-factor principal axis solution was chosen, and this accounted for 45.2% of the variance. Orthogonal and oblique rotations were applied to the solution, and inspection for the factor plots and the correlations between factors (table 2) suggested an oblique rotation was most appropriate. The factor pattern matrix is presented in table 3.

Inspection of the factor loadings (table 3) revealed that each factor had loadings for both the physical anxiety symptoms and the beliefs (fears). For factor 1, all items were associated with symptoms of faintness, diz-

TABLE 3. Factor Loadings and Communalities for Rotated Factors for 335 Patients With Anxiety Disorders

Symptom or Belief (Fear)	Factor				Communality
	1 (Vestibular Symptoms)	2 (Respiratory Symptoms)	3 (Psychological Threat)	4 (Autonomic Arousal)	
Faintness	<u>0.86</u>	0.02	0.01	0.03	0.79
Dizziness	<u>0.80</u>	-0.01	-0.00	0.08	0.70
Lightheadedness	<u>0.78</u>	0.04	0.08	0.00	0.67
Fear of fainting	<u>0.82</u>	0.08	-0.04	-0.08	0.63
Weakness in legs	0.37	0.02	-0.02	0.39	0.42
Choking feeling	-0.09	<u>0.81</u>	0.25	-0.00	0.67
Difficulty swallowing	-0.07	<u>0.79</u>	0.11	0.02	0.66
Difficulty breathing	0.09	<u>0.72</u>	0.00	0.00	0.57
Tightness or pain in chest	-0.00	<u>0.71</u>	-0.11	0.04	0.50
Fear of dying	0.19	<u>0.69</u>	0.05	-0.41	0.39
Feelings of unreality	0.28	-0.03	<u>0.78</u>	-0.17	0.71
Surroundings seem unreal	0.27	0.00	<u>0.77</u>	-0.19	0.69
Fear of losing control	-0.12	-0.03	<u>0.72</u>	0.18	0.57
Fear of going crazy	-0.06	0.25	<u>0.71</u>	-0.14	0.53
Fear of looking foolish	-0.32	-0.18	<u>0.49</u>	<u>0.55</u>	0.50
Sweating	0.03	-0.24	-0.16	<u>0.91</u>	0.60
Hot/cold flushes	0.08	-0.15	0.03	<u>0.70</u>	0.46
Trembling	-0.06	-0.08	0.10	<u>0.70</u>	0.46
Palpitations	-0.01	0.10	-0.04	<u>0.57</u>	0.37
Tingling in hands/feet	0.08	0.29	-0.03	0.34	0.34
Nausea	-0.01	0.16	-0.10	0.44	0.26

ziness, lightheadedness, and the feared consequence of fainting. This factor was labeled vestibular symptoms. The second factor had loadings for symptoms of respiratory disturbance and the fear of dying. All symptoms here could be interpreted as indicating threat to life. This factor was labeled respiratory symptoms. The third factor was made up of "unusual" symptoms of depersonalization and derealization plus with the fear of going crazy, losing control, and looking foolish. Beck et al. (7) suggested that an association between these apparently strange and uncontrollable anxiety symptoms and fear of loss of sanity and control should be found in panic attacks. This factor was labeled psychological threat. For the fourth factor, most of the symptoms were susceptible to external scrutiny, for example, flushes, sweating, and trembling. This factor could be labeled autonomic arousal. The feared consequence of looking foolish also loaded, suggesting that this factor may encompass what Beck et al. (7) called "sociality threats."

To assess the relationships between the beliefs and symptoms further, correlations were performed between the individual beliefs associated with each factor and the factors minus that belief. The correlations were greatest for the fear of fainting with vestibular symptoms ($r=0.57$), followed by fear of losing control ($r=0.42$) and fear of going crazy ($r=0.40$) with psychological threat, fear of dying with respiratory symptoms ($r=0.34$), and fear of looking foolish with autonomic arousal ($r=0.30$) and with psychological threat ($r=0.25$).

Factor scores were developed from each of the four factors by adding the raw scores of the variables with loadings greater than 0.45 on each factor and dividing by the number of loading variables (11). A multivariate analysis of variance was performed for the factors

across diagnoses. A linear combination of factors was derived that was significantly affected by diagnosis according to Wilks's lambda ($F=4.78$, $df=12$, 868, $p<0.001$). The canonical loadings for the single significant root ($\chi^2=55.87$, $df=12$, $p<0.001$) are presented in table 4. The largest weightings were for vestibular symptoms and faintness. A post hoc comparison between the diagnoses of panic disorder and agoraphobia revealed no significant differences on this linear combination ($F=1.48$, $df=4$, 331, n.s.), but a significant difference was found between the panic disorder and the non-panic-disorder diagnoses ($F=4.98$, $df=4$, 331, $p<0.001$).

DISCUSSION

This study provides support for a definition of fear of fear as catastrophic beliefs associated with the symptoms of anxiety. Unlike study groups used in other research in this area (8, 12), our subjects were clinic outpatients with anxiety disorders. Also, unlike other studies of fear of fear (5, 13), the present study found underlying dimensions of fear of fear suggesting that different fears are related to particular symptom clusters. The results do not support the findings of Reiss et al. (8) that fear of fear as assessed by the Anxiety Sensitivity Index is unidimensional. Rather, they are consistent with the finding of multidimensionality on this scale by Telch et al. (14). Also, the Agoraphobic Cognitions Questionnaire (5) has two factors—social/behavioral concerns and physical concerns—that are similar to the dimensions of fear found on the Anxiety Symptoms and Beliefs Scale. Our findings are consistent with the conceptualization by Beck et al. (7) of threats to domains of potential vulnerability that underlie the

TABLE 4. Factor Scores and Canonical Coefficients for Four Diagnostic Groups of Patients With Anxiety Disorders

Factor	Factor Score ^a								Canonical Coefficient ^b
	Panic Disorder		Generalized Anxiety Disorder		Agoraphobia		Social Phobia		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Factor 1 (vestibular symptoms)	3.64	1.05	2.20	1.17	3.17	1.25	2.32	1.22	0.60
Factor 2 (respiratory symptoms)	2.01	0.83	1.90	0.87	2.56	1.08	1.87	0.89	0.66
Factor 3 (psychological threat)	2.65	1.08	2.47	1.09	3.07	1.11	2.68	0.96	0.23
Factor 4 (autonomic arousal)	2.74	0.80	2.64	0.85	3.16	0.97	3.12	1.00	-0.30

^aSum of raw scores of variables with loadings greater than 0.45, divided by number of loading variables (11).

^bFrom MANOVA.

anxiety disorders, but they also suggest an extension in that particular symptom clusters are correlated with certain domains of threat and vulnerability.

Although the results show that the associations between symptoms and fears are present across the diagnoses of social phobia, generalized anxiety disorder, agoraphobia with panic attacks, and panic disorder, it appears that they are present in higher levels in agoraphobia. Fear of fear as assessed by the Anxiety Symptoms and Beliefs Scale is particularly severe for patients with agoraphobia with panic attacks. This is consistent with the views of Goldstein and Chambless (4) and Chambless et al. (5). More recently, Chambless and Gracely (15) found that fear of fear as assessed across anxiety disorder diagnoses by the Agoraphobic Cognitions Questionnaire and the Body Sensations Questionnaire was highest in agoraphobic subjects. One possible reason for this relationship is the association between fear of fear and avoidance (15, 16). It is possible that the extent of agoraphobic avoidance may represent the extent and severity of perceived threats and vulnerabilities. The relationship found between vestibular and respiratory symptoms and agoraphobia may be related to the more catastrophic outcomes associated with these symptoms. An agoraphobic patient who feels that experiencing respiratory symptoms leads to catastrophic physical outcomes may avoid situations where vulnerability to such threats would be high, such as crowds, shopping centers, public transportation, or places where help was not easily accessible. The same situations might also be avoided because of the threat to perceived social/behavioral competency but may not have the same level of threat associated with them. These results suggest that not all symptoms of anxiety are equally important to fear of fear. Vestibular symptoms and the fear of fainting and respiratory symptoms such as chest pain, difficulty breathing, and choking sensations, which could quite readily be misperceived as life-threatening, may be a part of the cluster of symptoms and beliefs associated with fear of fear. In contrast, trembling and shaking, which are obvious external expressions of lack of social adeptness, may be less open to catastrophic interpretation.

The limitation of this study is that it uses retrospective self-reports of anxiety symptoms in correlational analyses to investigate relationships between cognitive

appraisals of anxiety symptoms and fear. Furthermore, no conclusions can be drawn from these data with respect to the causal relationships that may exist among the physiological, cognitive, and affective components of fear of fear. It is possible that there are complex and dynamic relationships among anxiety symptoms, cognitions, and fears underlying the fear of fear in anxiety disorders (10).

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Toward a Brain Map of Auditory Hallucinations

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Objective: This study asks whether auditory hallucinations are reflected in a distinctive metabolic map of the brain. **Method:** Regional brain metabolism was measured by positron emission tomography with [^{18}F]-fluorodeoxyglucose in 12 DSM-III schizophrenic patients who experienced auditory hallucinations during glucose uptake and 10 who did not. All patients were free of neuroleptics and 19 had never been treated with neuroleptics. Nine patients were reexamined after 1 year to assess effects of neuroleptic treatment. **Results:** Compared with the patients who did not experience hallucinations, the patients who did experience hallucinations had significantly lower relative metabolism in auditory and Wernicke's regions and a trend toward higher metabolism in the right hemisphere homologue of Broca's region. Hallucination scores correlated positively and significantly with relative metabolism in the striatum and anterior cingulate regions. Neuroleptic treatment resulted in a significant increase in striatal metabolism and a reduced frontal-parietal ratio, which was significantly correlated with a decrease in hallucination scores. **Conclusions:** Auditory hallucinations involve language regions of the cortex in a pattern similar to that seen in normal subjects listening to their own voices but different in that left prefrontal regions are not activated. The striatum plays a critical role in auditory hallucinations.

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In order to discover the neural basis of psychotic phenomena such as auditory hallucinations, the systems of the living brain involved in their occurrence must be identified. Auditory hallucinations, a salient feature of 70% of schizophrenic psychoses, may represent subvocal speech. The notion that auditory hallucinations might reflect the subjects' own speech was suggested by the observation that the reported content of hallucinations corresponded with that recorded through a microphone held to the mouth (1). The fact that auditory hallucinations can be interrupted by opening the mouth very wide, thus preventing vocalization, suggests that the hallucinations are expressed by the subject's larynx

(2). We examined regional brain glucose metabolism in chronic schizophrenic subjects with persistent hallucinations (N=9) and compared them with a matched group of patients (N=10) and normal control subjects (N=10) (3). We reported that correlations between metabolism in certain language regions were significantly different in the hallucinating group than in the nonhallucinating group and control subjects. Hallucination scores correlated positively and significantly with relative metabolism in the anterior cingulate region. All patients were taking neuroleptic medications.

In the present study we examined metabolic activity in language regions of the brain (figure 1) with positron emission tomography (PET) using [^{18}F]-fluorodeoxyglucose (FDG) in 22 drug-free schizophrenic patients who experienced auditory hallucinations; 19 of the patients had never been treated with antipsychotic drugs. Twelve of the patients reported hearing voices during the period in which FDG was being taken up in the brain, and 10 did not. Thus, the relative regional metabolism of the brain was pictured and measured during the fortuitous occurrence of hallucinations in one group of patients, while in the other group, the voices were quiescent during the examination. Using unmedicated subjects, we could thus reexamine the hypothesis that hallucinatory events involve the language regions of the brain.

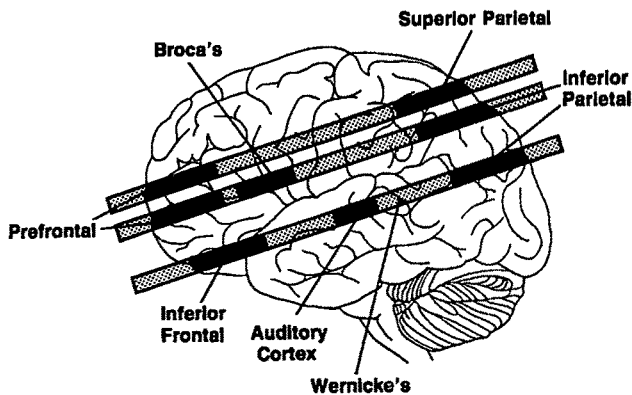
Presented at a new research session at the 143rd annual meeting of the American Psychiatric Association, New York, May 12-17, 1990. Received Nov. 6, 1990; revision received Jan. 8, 1992; accepted Feb. 7, 1992. From the Departments of Psychiatry and Biomedical Sciences, McMaster University; the Department of Psychiatry, University of Toronto, Toronto, Ont.; and the Department of Nuclear Medicine, Chedoke-McMaster Hospitals, Hamilton, Ont. Address reprint requests to Dr. Szechtman, Department of Psychiatry, McMaster University, 1200 Main St. West, Hamilton, Ont., Canada L8N, 3Z5.

Dr. Cleghorn died June 8, 1992.

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FIGURE 1. Three Slice Levels of the Brain Examined in 22 Schizophrenic Patients With and Without Auditory Hallucinations During PET Scan^a



^aLow: orbitofrontal-superior temporal including auditory cortex and an inferior part of Wernicke's region—inferior parietal; middle: prefrontal including Broca's region—parietal; high: prefrontal-supramarginal and parietal.

METHOD

Patients

We recruited patients from the emergency and outpatient services who met presumptive *DSM-III-R* criteria for schizophrenia. They were then admitted to the hospital and followed as outpatients for at least 1 year. Patients with a history of neurological disorder and major medical illness were excluded. Detailed developmental histories were obtained from family members. Histories included the onset of negative and later positive symptoms; this information, when combined with follow-up data, permitted the diagnosis of schizophrenia by *DSM-III* criteria.

It should be understood that the patients classified as not having hallucinations had experienced hallucinations at various times before the procedure. The mean age of the patients who did experience hallucinations during PET scan was 24.2 years ($SD=7.4$). Eight were men and four were women. Nine patients were reexamined after 1 year of neuroleptic treatment. Five had hallucinated during the scan, but all had auditory hallucinations before and after the scan. The patients who did not experience hallucinations during PET scan had a mean age of 29.5 years ($SD=9.7$). Eight were men and two were women. All but three patients were right-handed. The two left-handed patients and one mixed-handed patient were in the group that experienced hallucinations. Only two patients who did not and one patient who did experience hallucinations had in the past been treated with neuroleptic medications, and they had been drug free for many months before the study.

All patients had been ill for 6 months or more, some for many years. There was no significant difference between the groups' length of illness: the mean for patients who did experience hallucinations was 4.5 years

TABLE 1. Demographic Characteristics of Schizophrenic Patients With and Without Auditory Hallucinations

Item	Hallucinating Subjects (N=12)		Nonhallucinating Subjects (N=10)	
	Mean	SD	Mean	SD
Age (years)	24.2	7.4	29.5	9.7
Education (years) ^a	11.1	1.8	13.0	2.2
Length of medication (years)	0.8	2.6	1.0	2.1
Age at onset of schizophrenia (years) ^b	18.8	2.9	23.6	4.5
Length of illness (years)	4.5	5.5	5.9	5.8
Number of episodes	1.3	0.6	1.2	0.6
Use of street drugs ^c	1.2	0.8	1.0	0.8
Performance IQ ^d	98.1	14.6	105.4	12.6
Memory quotient ^e	81.6	18.8	99.4	17.2
Picture arrangement score ^f	7.7	2.5	10.9	3.1
SADS-C positive symptom scores ^g	3.0	1.0	1.9	1.0
SADS-C negative symptom scores ^h	4.3	0.8	2.0	0.8

^a $t=2.25$, $df=20$, $p=0.04$ (two-tailed test for all comparisons).

^b $t=3.00$, $df=20$, $p=0.007$.

^c1.0=prior substance abuse to a mild or moderate degree by *DSM-III* criteria.

^d $t=2.10$, $df=20$, $p=0.05$.

^e $t=2.31$, $df=20$, $p=0.03$.

^f $t=2.62$, $df=20$, $p=0.02$.

^g $t=2.80$, $df=20$, $p=0.01$.

^h $t=2.67$, $df=20$, $p=0.01$.

($SD=5.5$), and the mean for patients who did not experience hallucinations was 5.9 years ($SD=5.8$). However, the mean age at onset for the patients who did experience hallucinations was significantly younger than that of the patients who did not experience hallucinations during PET scan ($p=0.007$) (table 1).

The patients who experienced hallucinations also had significantly less education and a lower Wechsler performance IQ and memory quotient. Picture arrangement scores were significantly lower in the patients who experienced hallucinations (table 1). None of the 60 additional neuropsychological tests we used discriminated between groups. These measures are described in Cleg-horn et al. (4). Type I errors are possible here because of the large number of comparisons.

Both positive and negative symptoms were more severe among the patients who experienced hallucinations (table 1). The patients who experienced hallucinations had higher hallucination scores than those who did not experience hallucinations when measured before scanning (mean=4.3, $SD=0.8$, and mean=3.0, $SD=0.7$, respectively) as well as during the procedure (mean=4.1, $SD=1.2$, and mean=0, $SD=0$). Since hallucinations occurred more frequently in the patients who did experience hallucinations, there was a higher probability of their occurring during the scanning procedure.

Since group differences in brain metabolic data might reflect the severity of any of the symptoms or neurocog-

nitive impairments rather than the presence or absence of hallucinations during the scan, correlations between these variables and hallucination scores during scanning were calculated. None of the symptom scale scores, the mean positive and negative symptom scores, or neurocognitive measures were significantly related to hallucination scores during the scanning procedure or before it. Thus, these hallucinatory events are independent of the other measures but might well be related to factors underlying severity of illness. Since these factors might be reflected in regional brain metabolism, we examined the relation of all symptom scores to regional brain metabolism.

One clear difference between groups is that they did or did not hallucinate during the FDG uptake period before the scan. Hallucinations occur intermittently, while the other symptoms are more constant.

Procedure

Informed consent, following a full explanation of all procedures employed in the study, was obtained from all subjects. An experienced psychiatric nurse cared for the subjects and inserted a number 18 angiocatheter into a vein of the forearm. Subjects were injected with FDG, 5 mCi, while lying on a comfortable stretcher. They were instructed to keep their eyes closed and were not spoken to. The only noise was due to the air handling system of the building. Warming the arm produced arterialized samples of venous blood that were taken from the arm opposite that used for FDG injection for the determination of plasma glucose and FDG concentrations. Scanning was started 45 minutes after FDG injection. Local rates of cerebral glucose metabolism were calculated according to the method of Brownell et al. (5). The procedures and methods have been more fully described elsewhere (3, 6).

The Schedule for Affective Disorders and Schizophrenia—Change Version (SADS-C) (7) was administered immediately before the glucose uptake period by the nurse so that ratings of positive and negative symptoms, initially obtained on admission, could be checked. Scales for the assessment of five negative symptoms (Scale for the Assessment of Negative Symptoms) and four positive symptoms (Scale for the Assessment of Positive Symptoms) were 6-point scales in which each level of intensity was defined in behavioral terms (8) (table 1). The ratings are based on interview data and on behavioral observations by staff and family members. The patients were well-known to the highly experienced research nurse (S.F.).

Immediately before being placed in the tomograph, patients were asked to report any auditory hallucinations they had during the uptake period for FDG. These reports were recorded and reviewed together with an experienced clinician (J.M.C.), and a consensus rating was made. The mean hallucination score for the hallucinating patients was 4.1 (SD=1.2). A rating of 3 describes the hallucination as vivid, occasional, and both-ersome; a rating of 4, as vivid and frequent.

Local Cerebral Glucose Metabolism

Regional distribution of FDG was measured with the McMaster PET, which has a spatial resolution of 8 mm (full width at half maximum) in the plane and 12 mm in the axial direction (9). It can therefore resolve voxels of less than 1 cm³. At least 10⁶ counts were collected, in 3 minutes, for each slice. The subject's head was held in a Perspex restraining device. Alignment in the left-to-right axis was ensured by inspection of a preliminary scan taken at the level of the thalamus. Typically, 16 slices of the brain (on a plane 5° to the orbitomeatal line) were obtained sequentially from the level of the hippocampal gyri up to the level of cortical vertex. Although each slice was 15 mm thick, it overlapped its predecessor by 10 mm. With this procedure, the slice with greatest volume of gray matter of interest for each subject can be identified and selected. For this study, three slices were first selected for analysis (figure 1). The lowest slice (midthalamic-midstriatal slice) contained the largest amount of temporal cortex, thalamic, and striatal tissue; auditory cortex is defined as segments 10 and 11 (figure 2). The procedure for dividing the cortex into segments is shown in figure 2. The middle slice (midcallosal slice) passed above the basal ganglia through the midportion of the dorsoventral extent of the corpus callosum. Language regions of the brain were approximately located by transposing brain stimulation maps onto the PET image, as described by us (3), and are shown in figures 1 and 2.

Data Analysis

In order to test the hypothesis that language areas of the brain are involved in auditory hallucinations, the groups of patients who did and did not hallucinate during FDG uptake were compared. A two-way analysis of variance (ANOVA) was used to examine group and laterality differences and their interactions in each region of interest, followed by *t* tests (two-tailed) for post hoc comparisons. Frontal and parietal relative metabolism was later examined by using the same methods.

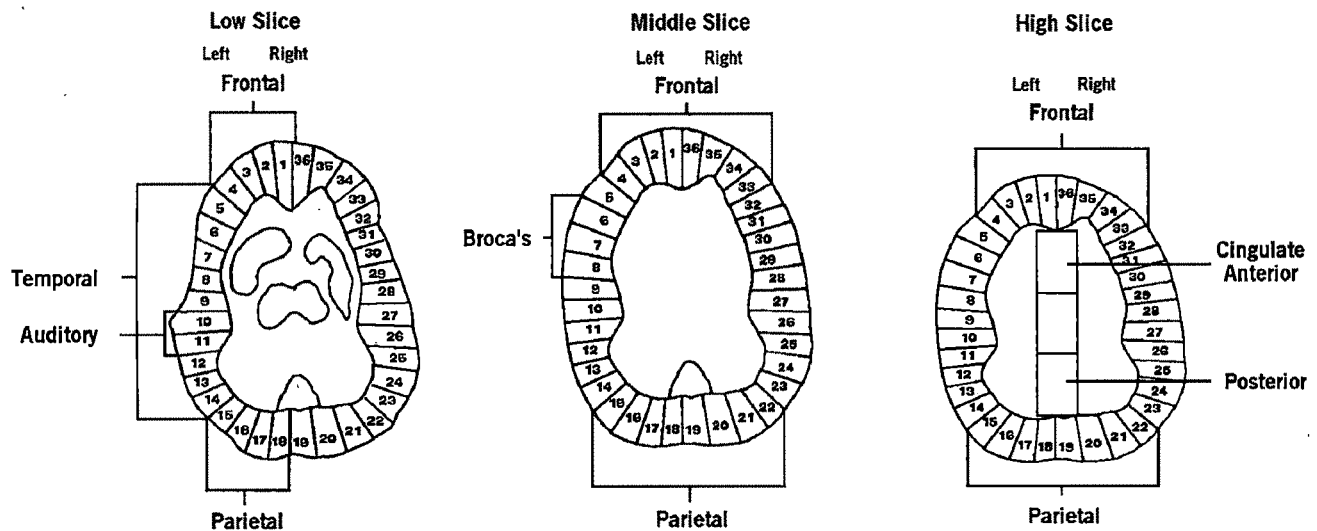
RESULTS

The groups did not differ significantly in absolute whole brain glucose metabolic rate: the mean for patients who did experience hallucinations was 34.50 $\mu\text{mol}/100 \text{ g}/\text{min}$ (SD=10.10), and the mean for patients who did not experience hallucinations was 32.40 $\mu\text{mol}/100 \text{ g}/\text{min}$ (SD=6.70). There were no significant differences between the means of tomographic slices within or between groups.

Relative Regional Metabolism and Laterality

To test the hypothesis that language areas of the brain are involved in auditory hallucinations, groups were compared by two-way ANOVA (Group by Laterality)

FIGURE 2. Cortical Rim, Divided Into 36 Segments Each Spanning an Arc of 10°, Examined in 22 Schizophrenic Patients With and Without Auditory Hallucinations During PET Scan^a



^aThe borders were defined by an edge-detecting algorithm. In the low slice central structures are corpus striatum and, to the posterior, thalamus. Auditory cortex is defined as segments 10 and 11 and Wernicke's region as segments 9–13. In the middle slice no structures are visible in the center of the brain. Broca's region is defined as segments 6–8 in that slice (see text). In the high slice the cingulate gyrus is visible, as well as the rim of the cortex.

and by *t* tests in each region in the temporal and supramarginal areas and Broca's regions in frontal cortex (figure 1). Since the striatum has a role in language, it was also included in the analysis. The results show trends toward higher relative metabolism in the right hemisphere regions homologous for Broca's and lower relative metabolism in primary auditory areas and in the right superior temporal region, which includes part of auditory association cortex, in the patients who did experience hallucinations. For the right hemisphere homologue of Broca's, the mean relative metabolism in the patients who did experience hallucinations was 1.04 (SD=0.04), and the mean in patients who did not experience hallucinations was 1.03 (SD=0.05) ($t=1.77$, $df=20$, $p=0.09$). For the right auditory, the mean in patients who did experience hallucinations was 1.03 (SD=0.05), and the mean in patients who did not experience hallucinations was 1.07 (SD=0.05) ($t=1.82$, $df=20$, $p=0.08$). For the right superior temporal, the mean in patients who did experience hallucinations was 1.01 (SD=0.04), and the mean in patients who did not experience hallucinations was 1.05 (SD=0.04) ($t=1.91$, $df=20$, $p=0.07$).

The differences reach significance in the posterior half of the superior temporal gyrus, the mean of regions 9–14 on the left and 23–28 on the right (figure 2) ($F=6.59$, $df=1$, 20 , $p=0.02$), with the patients who did experience hallucinations having lower relative metabolism (mean=1.03, SD=0.02) than patients who did not experience hallucinations (mean=1.05, SD=0.02). When the left-handed patients were removed from the analysis, the posterior temporal values were significantly lower in the patients who did experience hallucinations

(mean=1.03, SD=0.02) than in the patients who did not (mean=1.05, SD=0.02) ($F=8.74$, $df=1$, 17 , $p=0.009$). The mean of right and left auditory regions was also significantly lower in the patients who did experience hallucinations than in those who did not (mean=1.01, SD=0.03, $N=9$, versus mean=1.05, SD=0.04, $N=10$) ($F=6.42$, $df=1$, 17 , $p=0.02$).

There was also a significant Group by Laterality interaction in the anterior temporal region ($F=4.57$, $df=1$, 20 , $p=0.05$). When the three left-handed patients were removed from this analysis, the interaction became nonsignificant. An interaction between group and laterality in the striatum was significant whether or not left-handers were deleted ($F=4.78$, $df=1$, 20 , $p=0.04$); in patients who did experience hallucinations, the mean left relative metabolism was 0.98 (SD=0.09) and the mean right was 0.98 (SD=0.09); in patients who did not experience hallucinations the mean left relative metabolism was 0.94 (SD=0.08) and the mean right was 0.98 (SD=0.05).

There were no significant differences between groups in relative metabolism in supramarginal, frontal, or parietal regions or in the anterior or posterior cingulate gyrus or thalamus, as depicted in figures 1 and 2.

Correlations Between Symptom Scores and Relative Regional Metabolism

Hallucination scores correlated with striatum ($r=0.68$, $N=12$, $p<0.01$, one-tailed, Pearson product-moment correlation), left striatum ($r=0.69$, $p<0.01$), right striatum ($r=0.64$, $p<0.02$), and anterior cingulate ($r=0.52$, $p<0.05$). Hallucination scores or other symptom

TABLE 2. Correlations Between Relative Metabolism in Selected Brain Regions in Schizophrenic Patients With and Without Auditory Hallucinations During PET Scan

Brain Region	Correlation (r)		Probability of Significant Difference Between Correlations (Fisher's exact test)
	Hallucinating Subjects ^a (N=12)	Nonhallucinating Subjects ^a (N=10)	
Broca's with			
Middle slice, left supramarginal—posterior half ^b	0.59	-0.88	<0.001
High slice, left supramarginal	0.88	0.18	<0.05
Left auditory: low slice, left superior temporal	0.88	-0.03	<0.01
Right auditory			
Middle slice, left supramarginal	-0.74	0.32	<0.05
High slice, left supramarginal	-0.79	0.26	<0.01
Middle slice, left supramarginal			
High slice, left supramarginal	0.94	-0.08	<0.001
High slice, right supramarginal—posterior half	-0.85	0.43	<0.001
High slice, right supramarginal	-0.75	0.32	<0.05
Low slice, right posterior temporal	-0.83	0.17	<0.01
Middle slice, right supramarginal	-0.83	-0.18	<0.05
Middle slice, right supramarginal—posterior half ^c	-0.87	0.38	<0.001
Middle slice, right parietal	-0.71	0.64	<0.01
High slice, right parietal	-0.72	0.69	<0.001
High slice, left supramarginal			
Low slice, right superior temporal	-0.79	0.34	<0.01
Low slice, right superior temporal—posterior half	-0.84	0.46	<0.001
Middle slice, right supramarginal—posterior half	-0.84	0.06	<0.05
High slice, left supramarginal—posterior half			
Anterior cingulate	0.42	-0.76	<0.01
Middle slice, right supramarginal	-0.71	0.14	<0.05
High slice, right supramarginal—posterior half	-0.79	0.53	<0.001
High slice, right supramarginal	-0.88	-0.03	<0.05
Left striatum: middle slice, right supramarginal	-0.29	-0.87	<0.05
Middle slice, right supramarginal			
Middle slice, left supramarginal—anterior half	-0.69	0.14	<0.05
High slice, left supramarginal	-0.80	-0.10	<0.05
High slice, right supramarginal—posterior half: high slice, left supramarginal	-0.86	-0.25	<0.05
High slice, right frontal: middle slice, left parietal	-0.93	-0.47	<0.05

^aCorrelations of ± 0.50 in hallucinating subjects and ± 0.55 in nonhallucinating subjects were significant at $p=0.05$ or better (one-tailed).

^bWernicke's region.

^cHomologous for Wernicke's region.

scores were not significantly related to any of the regions of interest.

Neuroleptic Effects

Nine patients were reexamined after 1–2 years of neuroleptic treatment. We calculated correlations between change over the 1–2 years in relative metabolism and change in symptom scores ($N=9$). The decrease in hallucination scores was significantly related to a decrease in high frontal values ($r=0.89$, $p<0.01$) and an increase in high right parietal values ($r=0.84$, $p<0.01$). Reduced hallucination scores were also correlated with a reduction in the frontal/parietal ratio ($r=0.89$, $p<0.01$). These changes may be reciprocal, since they are based on changes in the same tomographic slice. The metabolic data are ratio data and share the same denominator. The reduction in total positive symptom scores was associated with increased values in striatum ($r=0.90$, $p<0.01$).

Correlations between brain regions were significantly different in patients who did experience hallucinations than in those who did not in seven of 18 regions meas-

ured ($p<0.01$, Fisher's exact test) (table 2). Correlations in the patients who did experience hallucinations were not significantly different from those in the healthy control subjects ($N=30$). The pattern of regional correlations within hallucinating patients resembled that in healthy control subjects, while the pattern in nonhallucinating patients did not.

DISCUSSION

Relative metabolism in the posterior superior temporal regions of both hemispheres was significantly lower in patients who hallucinated compared to those who did not hallucinate during FDG uptake before scanning. Similarly, the auditory region on the right showed a trend in the same direction, as did the right hemisphere homologue for Broca's region. Right/left ratios in the anterior temporal and striatal regions were significantly lower in the hallucinatory state.

When left-handed subjects were removed from the analysis, the regional differences were greater and the left/right asymmetry differences were smaller. Since we

do not know whether the left-handed subjects had language represented in the right hemisphere, we cannot say which analysis is better.

The lack of convincing differences in other language regions is consistent with the findings of Buchsbaum et al. (10), who compared patients who did experience hallucinations with those who did not in their initial work on hypofrontality, and with our study of chronic, medicated hallucinating patients (3), whose indifference to hallucinatory experiences suggested to us that they were not attending to their voices. This lack of statistical power may also reflect the weakness of the stimulus: auditory hallucinations occurred intermittently during the 45-minute uptake period. When the data are compared with language stimulation studies in normal subjects (see following discussion), a stronger effect might be expected if the stimuli (hallucinations) occupied more of the uptake time. Studies with ^{15}O labeled water, whose half-life is 2 minutes, may make this possible.

We examined the data for possible confounding effects of differences between patients who did and did not experience hallucinations in symptom severity and cognitive impairment. The fact that neurocognitive deficits were more severe in the patients who did experience hallucinations than in those who did not supports the data on symptoms suggesting that the patients who did experience hallucinations were more severely ill in both domains. These domains appear to be separate, since we have not found any significant relations between symptom scores and neurocognitive scores in our studies, even when these patients were included in a larger sample ($N=27$) (11). Cognitive test scores are not significantly related to glucose metabolism in language regions. Rather, scores on tests of registration of information covary positively with the level of frontal metabolism (11).

None of the symptoms other than hallucinations was related to glucose metabolism in language regions. Furthermore, none of the other symptom scores was significantly related to hallucination scores.

In the striatal and cingulate regions relative metabolism was positively and significantly correlated with hallucination scores in the patients who did experience hallucinations. In our previous study of chronic hallucinating patients, we also observed that hallucination scores correlated positively and significantly with anterior cingulate relative metabolism (3). In that chronic, neuroleptic-treated patient group, however, the striatal metabolism was not statistically implicated—a finding that can be understood in that neuroleptics significantly alter striatal relative metabolism (12). These correlations are in contrast with the report of Mathew et al. (13) of negative correlations of hallucination scores on the Brief Psychiatric Rating Scale with cerebral blood flow (CBF) in left parietal, left temporal, right temporoparietal, and right occipital cortices.

We failed to replicate differences between the groups in correlations between certain language regions that we reported in chronic medicated schizophrenic sub-

jects (3). Although seven of 18 correlations between language regions differentiated patients who did experience hallucinations from those who did not, the analysis of correlations between regions in a new control group ($N=30$) demonstrated no difference between patients who did experience hallucinations and control subjects. Thus, in this population, correlational analysis did not reveal a pattern characteristic of the hallucinatory process.

Prior substance abuse was an important factor in the chronic patient study in that substance abuse ratings correlated with hallucination scores ($r=0.53$, $p<0.01$) and with left anterior temporal metabolism ($r=0.59$, $p<0.01$). Substance abuse was not significantly related to hallucination scores or regional brain metabolism in the present study. It is possible that substance abuse aggravates auditory hallucinations through different pathways than those which usually mediate auditory hallucinations in schizophrenia.

Musalek et al. (14) have recently reported CBF changes during auditory hallucinations. CBF was measured by single photon emission computerized tomography in neuroleptic-treated patients with chronic auditory hallucinations that had resisted treatment. Hallucinations were associated with significantly increased blood flow in the anterior basal ganglia and medial temporal areas and relative frontal hypoactivity. In that study, p was set at 0.05 despite multiple comparisons and a study group of 17 subjects. If we had allowed this statistical criterion, our results might have been similar. Our data are, in general, consistent in implicating basal ganglia and temporal regions but not frontal hypoactivity.

A role for the striatum in auditory hallucinations is strongly supported by our data. Hallucination scores correlated positively and significantly with striatal relative metabolism. We have previously reported that neuroleptic treatment significantly reduces hallucination scores while significantly increasing striatal metabolism (15), and we now have shown that these two processes are related to a statistically significant degree. Change in frontal and parietal regions are also related to improvement in hallucinations, but these regions were not implicated at the time the hallucinations occurred. Nevertheless, it is possible that the significant increase in parietal metabolism and the decrease in frontal metabolism, which was correlated with a decrease in hallucination scores, could reflect a shift in attention from internal to external events.

Our studies, discussed earlier in this paper, and the evidence that auditory hallucinations can be stopped by immobilizing the larynx by opening the mouth wide (2) and by speaking or writing provide strong evidence that language mechanisms are involved in auditory hallucinations. How do auditory hallucinations differ from normal language?

Studies in normal subjects have presented language stimuli repeatedly and throughout the period of radiotracer uptake before PET scanning. Listening to monosyllabic words and phonemes (16) and to a com-

plex story (17) activates left perisylvian regions. Tasks that require semantic interpretation activate left inferior frontal (including Broca's) and anterior cingulate regions. Complex tasks also involve superior prefrontal activity (18, 19). This is not the pattern during auditory hallucinations, however.

Wernicke's region and auditory cortex showed significantly lower relative metabolism in hallucinating patients, while the right hemisphere homologue of Broca's region showed a nonsignificant trend toward activation. This same pattern in Wernicke's region has recently been observed in a PET CBF ^{15}O study by Frith et al. (20). Subjects required to speak words aloud showed suppression of Wernicke's regional blood flow (and activation in left prefrontal cortex). Thus, the pattern we observed is similar in part to that seen in subjects speaking and listening to their own voices. This is consistent with electrocortical observations in monkeys (21). Auditory cortex was activated in animals while they listened to a tape recording of their own voices but not while they vocalized. The failure to activate left prefrontal cortex including Broca's region may reflect the lack of intentionality characteristic of hallucinated language.

In addition, the striatum is implicated. While PET studies of language in normal subjects (16–18) do not mention the striatum, striatal lesions can contribute to aphasia (22, 23) and indirectly disrupt cortical processes involved in perceptual organization of auditory stimulation (24). We suggest that future studies determine whether auditory hallucinations involve the striatum to a greater extent than do normal listening and speaking.

An abnormality in the striatum might lead to hallucinations, since it is a repository of overlearned behaviors and is known to be involved in intermittent involuntary movements. Hallucination can be seen as involuntary thought and language events. Furthermore, PET studies suggest that the striatum may be the principal site of action for neuroleptics that usually ameliorate hallucinations (12).

In addition, patients who experience hallucinations are characterized by failure to discriminate the location of sounds, which may underlie the failure of reality discrimination with respect to the location of the speaker's voice (25). We may not have adequately measured metabolism in the right inferior parietal region, which subserves that locating function (26). Furthermore, the anterior cingulate is required for discriminating intended vocalizations from other auditory stimuli (27) and appears to have a role in auditory hallucinations in the present study and our previous study (3) in that the intensity of hallucinations and relative metabolism in the anterior cingulate are positively and significantly correlated.

In summary, comparison of our data on hallucinating patients with data on regional brain metabolism in normal language suggests that future studies compare auditory hallucinations and language task involvement of striatum, anterior cingulate, and parietal cortices and Broca's and Wernicke's regions. A picture of the hallu-

inating brain may thus be constructed and errors in the processes of generating and listening to language may be identified.

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Are Males More Likely Than Females to Develop Schizophrenia?

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Objective: This study was undertaken to determine whether the incidence of schizophrenia is equivalent for males and females. **Method:** An attempt was made to identify every first-episode case of psychosis in a large Canadian city over a period of 2½ years. A comprehensive referral network was established that included hospital and community settings where psychotic persons might appear. More than 300 potential subjects were identified, 175 of whom underwent a structured psychiatric interview and were assigned diagnoses according to five different diagnostic systems. **Results:** The incidence of schizophrenia was two to three times higher among males than among females. Even though the use of different diagnostic systems yielded slightly different risk rates, the elevated risk for males remained consistent. There were no differences between the sexes in the incidence of affective psychosis. In comparison with schizophrenia, the incidence rates for mood disorders with psychotic features were sometimes lower and sometimes higher, depending on the diagnostic system used. **Conclusions:** The findings, coupled with reports in the past 10 years from other investigators, challenge the conventional belief that the incidence of schizophrenia is the same for the two sexes.

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Knowledge about the sex distribution of psychosis among adults is important for several reasons. Because males and females differ in biology, rate of maturation, social status, and duration and types of experiences encountered, differences in the proportion of males and females afflicted with a disorder can suggest etiological clues (1). Moreover, males are more likely than females to develop psychoses in childhood. Whether this pattern continues with increasing age, thus suggesting that males are more vulnerable to severe psychopathology even in adulthood, is also of great interest.

Although authorities have long agreed that the prevalence and incidence of schizophrenia are the same for both sexes (2, 3), surveys in the past 10 years have provided inconsistent results. While studies in Asia (4), Europe (5-8), and North America (9, 10) have suggested an excess of schizophrenia among males, the Na-

tional Institute of Mental Health (NIMH)-sponsored Epidemiological Catchment Area (ECA) survey suggested that among noninstitutionalized populations, rates of schizophrenia are higher among women than among men (11). The World Health Organization (WHO) study of the incidence of schizophrenia (12) demonstrated no consistent pattern of male-female differences across sites. Studies of mood disorder have been more consistent in suggesting that men and women have an equal risk of developing bipolar disorder but that women have higher rates of major depressive disorder (13). However, studies of major depressive disorder have not differentiated between the relatively small percentage of individuals who have affective disorder with psychotic features and those who have affective disorder in general.

This report examines sex ratios in a broadly based sample of persons suffering a first episode of psychosis. First-episode subjects are particularly well suited for the study of sex differences. Studies that examine chronic patients risk confounding estimates of the sex distribution with sex differences in the course of psychotic illness, which is known to be more severe in schizophrenic men (14).

To avoid potential bias associated with reliance on institutionalized patients from a single setting, subjects were recruited from multiple sources both within and outside the traditional mental health care system. The project goal was to come as close as possible to obtaining a sample of all residents in a major Canadian coastal city who were experiencing psychotic symptoms

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for the first time in their lives. Since diagnostic criteria might influence estimates of relative risk, we compared male and female incidence rates (based on the number of new cases identified each year) using different diagnostic systems. To our knowledge the present study is the first to explore sex distributions in a large, community-based, diagnostically heterogeneous sample of first-episode psychotic patients.

METHOD

Subjects were recruited in Vancouver, B.C., Canada, from a metropolitan catchment area of approximately 480,000 persons. The referral network included all psychiatric hospitals and psychiatric services of general hospitals, university and college counseling services, community mental health centers, psychiatrists in private practice, private counseling services, employment and immigration counseling services, and a random sample of one-sixth of all general practitioners in Vancouver. About 18% of the referrals were from other than inpatient hospital services, including 9% from community mental health centers, 7% from private practice clinicians and community agencies, and 2% from hospital outpatient services. Over a period of 2½ years beginning in 1982, we identified a total of 318 potential subjects for our study. Of these, 31 terminated contact with their referral source or disappeared before we could contact them, and 94 refused to be interviewed. Although these 125 nonparticipants were not entered into our study, we were able to ascertain their ages, sex, and the diagnoses assigned by the referral sources. An additional 18 subjects agreed to participate but were dropped when they were found not to be psychotic or to be ineligible because they had experienced a previous episode of psychosis. Thus, 175 individuals, all of whom were experiencing their first lifetime episode of psychosis, gave informed consent to participate in the study.

To cast as wide a referral net as possible, we supplied our referral agencies with a broad definition of potential cases, including persons 1) who were currently psychotic (i.e., experiencing hallucinations or delusions, displaying grossly disorganized behavior, showing marked thought and speech disorder, or having two of the following symptoms: marked loss of drive, social withdrawal, severe excitement, overwhelming anxiety or fear, and gross self-neglect) and 2) who had not been treated before the present episode with antipsychotic, antimanic, or antidepressant drugs. Other inclusion and exclusion criteria required 1) that the subjects had lived in the Vancouver metropolitan area for at least 6 months, 2) that they were between 15 and 54 years of age, and 3) that they did not have an organic cerebral illness, severe mental retardation, a chronic physical disorder, or chemical dependence. A psychiatrist or clinical psychologist examined all potential subjects, including doubtful and borderline cases, initially recruited for the study using a structured psychiatric in-

terview (the Present State Examination) (15). Information from the psychiatric interview, reviews of clinical charts, and interviews with family members and friends was brought to case conferences attended by the project staff, including at least two experienced diagnosticians; this process resulted in a "best estimate" diagnosis (16) for each subject.

We used five different diagnostic systems, which varied in the breadth of their definition of schizophrenia, to classify participants: *DSM-III*, *ICD-9*, the Research Diagnostic Criteria (RDC) (17), the Feighner et al. criteria (18), and the 12-point flexible system of Carpenter et al. (19). With the exception of *ICD-9*, each of these systems has an explicit set of criteria for making diagnoses. To adapt the fairly loose *ICD-9* psychotic disorder categories for research purposes, the project clinicians used a checklist of symptoms and diagnostic criteria derived from the clinical constructs described in the *ICD-9* manual.

To ensure that subjects received the most accurate diagnoses possible, all symptoms and diagnostic criteria associated with the psychotic disorders described in each diagnostic system were reviewed for each patient to determine whether each symptom was present or absent. Then the diagnostic algorithms specified for each system (or the descriptive guidelines presented in *ICD-9*) were strictly followed to arrive at a diagnosis. Only subjects who satisfied the criteria for an active psychotic disorder in at least one diagnostic system were retained for study.

RESULTS

To determine whether an excess of patients of either sex was present in a category or group, we used chi-square tests to compare observed frequencies against the a priori expectation that the sexes would be equally represented. Among the 175 participants, who ranged in age from 16 to 50 years (mean=25.0 years, SD=7.8, for males; mean=25.7 years, SD=8.9, for females), 68% (N=119) were male, a proportion that deviated significantly from the expected rate of 50% (goodness-of-fit $\chi^2=22.68$, df=1, $p<0.001$). The percentage of male participants by diagnostic category within each diagnostic system is presented in table 1. The diagnostic systems are ordered such that the one with the broadest definition of schizophrenia (*ICD-9*) is on the far left. As table 1 shows, the broadest categorization resulted in a total rate of schizophrenia (114 cases) that was almost three times higher than that found when the most stringent diagnostic approach was used (41 cases according to the criteria of Feighner et al.). Regardless of the diagnostic system used, about three-fourths of all cases of schizophrenia involved males. Subjects with *DSM-III* schizophreniform disorder and RDC schizoaffective disorder were also disproportionately male.

The number of patients with mood disorders also varied depending on the diagnostic system used. *DSM-III* identified the largest number and the criteria of

TABLE 1. Incidence of Psychotic Disorders Among Male Subjects According to Five Diagnostic Systems

Disorder	ICD-9 ^a			12-Point System (Carpenter et al.)			RDC			DSM-III			Criteria of Feighner et al.		
	Total N	Male Subjects		Total N	Male Subjects		Total N	Male Subjects		Total N	Male Subjects		Total N	Male Subjects	
		N	%		N	%		N	%		N	%		N	%
Schizophrenia	114	85	75 ^b	70	53	76 ^b	64	48	75 ^b	54	41	76 ^b	41	30	73 ^c
Schizophreniform disorder	—	—	—	—	—	—	—	—	—	31	22	71 ^d	—	—	—
Schizoaffective disorder	—	—	—	—	—	—	54	38	70 ^c	6	5	83	—	—	—
Mania	28	15	54	—	—	—	25	14	56	38	20	53	16	8	50
Depression	23	12	52	—	—	—	20	11	55	35	23	66	21	11	52
Other ^e	10	7	70	105	66	63 ^d	12	8	67	11	8	73	97	70	72 ^b

^aFor ICD-9, "mania" refers to manic-depressive disorder, manic; "depression" refers to manic-depressive disorder, depressed.

^bProportion of males differs significantly from 50% ($p < 0.001$).

^cProportion of males differs significantly from 50% ($p < 0.01$).

^dProportion of males differs significantly from 50% ($p < 0.05$).

^eIncludes delusional and reactive psychoses in ICD-9 and DSM-III and unspecified psychoses in the 12-point, RDC, and Feighner et al. systems.

TABLE 2. Incidence of Psychotic Disorders (per 100,000 population) for Males and Females and the Male-Female Risk Ratio According to Five Diagnostic Systems

Diagnostic System	Schizophrenia	Schizophrenia-Related Disorders ^a	Total Schizophrenia and Schizophrenia-Related Disorders	Mood Disorders
ICD-9				
Males	10.90	—	10.90	5.06
Females	4.12	—	4.12	4.51
Risk ratio	2.64 ^b	—	2.64 ^b	1.12
12-point system (Carpenter et al.)				
Males	6.81	—	6.81	—
Females	2.55	—	2.55	—
Risk ratio	2.67 ^c	—	2.67 ^c	—
RDC				
Males	7.59	3.50	11.09	4.67
Females	2.55	1.57	4.12	4.32
Risk ratio	2.98 ^b	2.23 ^d	2.69 ^b	1.08
DSM-III				
Males	6.81	4.09	10.90	7.01
Females	1.96	1.77	3.73	5.30
Risk ratio	3.47 ^b	2.31 ^d	2.92 ^b	1.32
Criteria of Feighner et al.				
Males	5.64	—	5.64	2.92
Females	1.72	—	1.72	3.53
Risk ratio	3.20 ^c	—	3.20 ^c	0.83

^aIncludes schizophreniform disorder and schizoaffective disorder.

^bGoodness-of-fit chi-square significant ($p < 0.001$).

^cGoodness-of-fit chi-square significant ($p < 0.01$).

^dGoodness-of-fit chi-square significant ($p < 0.05$).

Feighner et al. the smallest number. Patients with psychotic mood disorders, however, were not significantly more likely to be of one sex than the other. Regardless of diagnostic approach, the number of subjects with a first episode of manic psychosis approximately equaled the number with a first episode of depression.

Our data make it possible to compare the frequency with which a first episode of psychosis was likely to be

mood related (depression or mania) or fall within the schizophrenia spectrum (schizophrenia, schizophreniform disorder, or schizoaffective disorder). If we assume that these two types of psychosis are equally probable, the results show that schizophrenia-spectrum psychoses predominated according to ICD-9 (goodness-of-fit $\chi^2 = 24.05$, $df = 1$, $p < 0.001$) and the RDC ($\chi^2 = 32.69$, $df = 1$, $p < 0.001$) but that the two classes of psychosis occurred with equal frequency according to the DSM-III and Feighner et al. criteria.

Examining the distribution of the sexes with the expectation that their numbers should be equal is open to potential error. First, this expectation, largely derived from prevalence data, may not pertain to incidence. Second, it fails to take into account possible differences in the numbers of males and females at risk in the general population. The population at risk—that is, persons between the ages of 15 and 54—was determined from Canadian census figures and consisted of 241,217 males and 239,185 females. The number of cases of disorder per year was calculated by dividing the number of cases by the period (in years) over which cases were recruited. The result was then divided by the number of individuals at risk to yield an estimate of 1-year incidence per 100,000 population. Incidence data, along with the male-female risk ratio, for the subjects with schizophrenia, schizophrenia-related psychoses (schizophreniform and schizoaffective disorder), and mood disorders are presented in table 2. These data are consistent with those in table 1 in suggesting that regardless of diagnostic approach, the incidence of schizophrenia is greater in males than in females. By contrast, there were no differences between the sexes in the incidence of affective psychosis.

It is unlikely that the persons who refused to participate or did not participate can account for the findings. Comparing participants with nonparticipants on age, sex, and diagnosis revealed few differences between the groups. The nonparticipants were about the same age as the participants (range=16–49 years; mean=25.1 years, $SD = 8.3$, for males; mean=27.1 years, $SD = 9.0$, for females); and although the participants were slightly

less likely to be male (58%), the total sample of participants and nonparticipants was 64% male, a proportion that still differs significantly from the expected 50% ($\chi^2=21.87$, $df=1$, $p<0.001$). The data also indicated that there was little difference between the diagnoses assigned to participants and nonparticipants by the referring agencies, all of which were using *DSM-III* or *ICD-9* at the time this study was conducted.

The incidence (per 100,000 population) of schizophrenia-related psychoses among nonparticipants was 8.95 for males and 5.30 for females. Although these referral-source diagnoses were probably less trustworthy than those made by the project diagnosticians, adding these cases to those of the project participants diagnosed according to narrow and broad definitions of schizophrenia provides an opportunity for a rough examination of risk ratios in the entire sample of possibly schizophrenic persons. When the nonparticipants with schizophrenia-spectrum psychoses are added to the participants with *DSM-III* diagnoses, the incidence figures are 15.76 and 7.26 for males and females, respectively, and the risk ratio is 2.17 (goodness-of-fit $\chi^2=16.41$, $df=1$, $p<0.001$). When these nonparticipants are added to the participants with the *ICD-9* diagnosis of schizophrenia, the corresponding figures are 19.85, 9.42, and 2.11 (goodness-of-fit $\chi^2=19.44$, $df=1$, $p<0.001$). Hence, even when the nonparticipants are taken into account, males still exhibit a higher incidence of schizophrenia-spectrum diagnoses than females.

DISCUSSION

The incidence of schizophrenia reported in this study is similar to that found in other surveys (20), including the WHO incidence study (12), the design of which was similar to that of our investigation and which also used subjects between the ages of 15 and 54. Our results demonstrate a higher incidence of schizophrenia and related disorders among males, but no differences between the sexes in the incidence of psychotic affective disorders. Our results for schizophrenia are consistent with several reports (all since 1984) indicating a higher incidence of schizophrenia among men than among women. NiNullain et al. (7), in an investigation of first admissions in three Irish counties, found that depending on the breadth of the criteria used to diagnose schizophrenia, 59%–68% of the subjects were male. These investigators also reported data indicating that on the basis of 1983 first-admission statistics for all of Ireland, the male-female risk ratio for schizophrenia was 1.50. Bland's report (9) of the rate of first admissions for schizophrenia in Canada indicated a risk ratio of 1.41. Even higher figures were found in Nottingham, England, for schizophrenia diagnosed according to *DSM-III* (risk ratio=2.43) (5) and in Denmark (risk ratio=2.29) (6). In their study of the incidence of schizophrenia in four Canadian provinces, Wattie and Kedward (10) found that 60% of their subjects were male. Stromgren (8) noted that despite a decrease in the over-

all incidence of schizophrenia from 1970 to 1984 in Denmark, for each calendar year the number of males succumbing to a first episode of schizophrenia was consistently higher than the number of females. Finally, in the WHO eight-center study of the incidence of schizophrenia (12), when paranoid and certain reactive states were excluded from the schizophrenia spectrum, six of the eight sites reported an excess of males. Only Moscow and an urban setting in India deviated from this pattern. Taken together with our findings, all of these reports challenge the conventional belief that the incidence of schizophrenia is equal for both sexes.

One possible explanation for these observations of an excess of males with schizophrenia stems from the hypothesis that the criteria for the diagnosis of schizophrenia have been narrowed. This phenomenon could lead to more men being diagnosed as schizophrenic and more women—since they are more likely to have affective features (13)—being diagnosed as having mood disorders (21). However, we found that differences between the sexes in incidence were the same regardless of the breadth or narrowness of the diagnostic criteria. Other investigations that have examined the incidence of schizophrenia as a function of breadth of the diagnostic criteria (5, 7) have also failed to find that narrowing the criteria leads to an excess of males with the diagnosis.

The excess of male schizophrenic subjects in our sample might have resulted from our elimination of females with this disorder who failed to meet our eligibility criteria. Compared with men, women with schizophrenia tend to be diagnosed at later ages (13, 22). Since women with psychiatric disorders are more likely than men to seek help from family physicians (23, 24), it is possible that some females who were potentially eligible for our project had received treatment at some point in their lives before they came to the attention of the mental health system and thus were disqualified from our study. This seems unlikely, however, because the patients who were referred to but did not participate in the study were not screened for prior treatment and yet were still predominantly male.

Other investigations, notably the WHO study of incidence (12), have used similar exclusion criteria. However, since these studies did not report data on noneligibility or refusal rates, comparisons are impossible. We were able to identify virtually all individuals with a first episode of psychosis, whether they participated in the study or not, who were involved with the inpatient or outpatient mental health care system or who appeared in other service settings in our catchment area. While it is possible that there were private practice physicians treating first-episode female psychotic patients who did not require hospitalization and who were not referred to our study, we have no reason to suspect that our data would differ from those of other investigators for this reason, since such cases would be unavailable at any site. Nevertheless, because of limitations to the thoroughness with which we could identify cases, studies such as ours leave open the possibility that women

with milder, less disruptive schizophrenia were missed. Because of this possibility, our report is better able to provide grounds for raising the question posed in its title than to answer the question definitively.

If our findings are correct, they may have implications for understanding the etiology of schizophrenia. If males are more susceptible to schizophrenia, this fact, coupled with their tendency to show an earlier age at onset (22) and a more debilitating course (14), suggests that males may be more biologically vulnerable and less able to adapt to psychosis than females. The sexes differ in their anatomy and physiology, processes of biological maturation, social status, occupational attainment, and duration and types of psychosocial experiences encountered. Examining variables related to such factors may provide valuable clues to understanding how schizophrenia develops.

Although data on the incidence of mood disorders exist, to the best of our knowledge, our study is the first to focus on first-episode cases with manifest psychotic features. Our results demonstrate that these disorders are distributed about equally across the sexes, a finding that does not depend on the breadth of the criteria used to diagnose these disorders. However, the diagnostic criteria do seem to influence the likelihood of receiving a mood- or schizophrenia-related diagnosis. The two systems with the broadest definitions of schizophrenia that also provided for the diagnosis of mood psychosis (ICD-9, RDC) identified significantly more schizophrenia-related disorders than mood disorders. With the DSM-III and Feighner systems, there was only a slight, nonsignificant trend for schizophrenia-related disorders to outnumber mood disorders.

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Painful Sensory Symptoms in Neuroleptic-Induced Extrapyramidal Syndromes

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Objective: The authors tested the hypothesis that neuroleptic-induced extrapyramidal syndromes are associated with painful sensations objectively conforming to the characteristics of primary sensory symptoms as reported in idiopathic and postencephalitic parkinsonism. **Method:** The frequency of subjective painful sensory symptoms and their relation to neuroleptic-induced extrapyramidal syndromes were examined in a consecutive series of 107 psychiatric patients newly admitted to acute care units at a teaching hospital. Patients without illnesses or conditions likely to be associated with pain were included in the study if they had a diagnosis other than organic mental syndromes and were receiving psychotropic medications as prescribed by their treating physicians. Structured interviews with a modified version of the McGill Pain Questionnaire to assess sensory complaints and neurological examinations for neuroleptic-induced extrapyramidal syndromes (parkinsonism and akathisia) were conducted independently by two raters blind to each other's findings and patients' medication status. **Results:** Fourteen (23%) of 60 patients receiving neuroleptics reported experiences of spontaneous pain subjectively attributed to pharmacological treatment, compared with only one (2%) of 47 patients receiving psychotropic medications other than neuroleptics. There was no difference between these two groups in subjective complaints of paresthesia (8% versus 9%). Twelve (55%) of the 22 patients with neuroleptic-induced extrapyramidal syndromes reported pain, compared with only two (5%) of the 38 patients who received neuroleptics but did not experience extrapyramidal syndromes. **Conclusions:** Although consonant with the study hypothesis, these results should be regarded as preliminary and interpreted conservatively in the light of the methodological limitations of the study.

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It is well established that a substantial proportion (about 40%) of patients suffering from postencephalitic or idiopathic parkinsonism experience distressing and ill-defined sensations that cannot be attributed directly to disorders of the musculoskeletal system, antiparkinsonian medications, peripheral neuropathy, or gross pathology of sensory pathways of the brain (1-5). These are commonly referred to as primary sensory symptoms, to distinguish them from sensory manifestations that may be attributed to disorders of the musculoskeletal system and therefore considered secondary. Subjective accounts of these disagreeable sensations vary widely, and some patients may have unusual

difficulties in describing them, perhaps because of a lack of comparable sensations associated with common diseases and life experiences (4). Nevertheless, primary sensory phenomena in parkinsonism have been readily classified into paresthesias and pain, the former including sensations of burning, coldness, tingling, and numbness and the latter comprising poorly localized painful sensations without thermal or anesthetic characteristics and not associated with increased muscle contraction or affected by movements or pressure (4). The pathophysiology of primary sensory symptoms in parkinsonism remains unknown, although it is believed that they result from central dopaminergic deficiency in the basal ganglia or other systems as a consequence of the disease process (2, 4, 6).

Parkinsonism and akathisia often occur in patients receiving neuroleptic drugs and are believed to be caused, at least in part, by the blockade of postsynaptic dopamine receptors (7). These neuroleptic-induced extrapyramidal syndromes share phenomenological, pharmacological, and biochemical characteristics with both idiopathic and postencephalitic parkinsonism (8, 9). In

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addition, there is evidence that at least some patients with neuroleptic-induced parkinsonism, particularly those who are elderly, may have underlying Parkinson's disease (10, 11). Thus, it is conceivable that neuroleptic-induced extrapyramidal syndromes may also be associated with primary sensory symptoms. The aim of this study was to test this hypothesis, first by examining the frequency of primary sensory symptoms in patients receiving neuroleptics compared with patients receiving psychoactive drugs other than neuroleptics, and then by contrasting the frequency of these sensory symptoms in patients with neuroleptic-induced extrapyramidal syndromes and patients without neuroleptic-induced extrapyramidal syndromes.

METHOD

The study group comprised 107 consecutive voluntary psychiatric inpatients recruited from five acute care units at an urban teaching hospital. Patients were included in the study if they had been newly admitted, had a psychiatric diagnosis other than organic mental syndrome, and were currently receiving psychotropic medications as prescribed by their treating physicians. Patients with a history of alcohol or substance abuse, neurological illnesses, musculoskeletal conditions (arthritis, muscle spasms), diabetes, and vascular disease and those concurrently being treated with ECT were excluded.

At the time of assessment, 60 patients were receiving neuroleptics, and 47 were receiving psychotropic drugs other than neuroleptics. In the patients receiving neuroleptics, haloperidol and trifluoperazine were the most frequently prescribed drugs, each compound accounting for about 30% of the patients. Chlorpromazine was administered to about 20% of patients, and the remaining patients received several other neuroleptics. The mean length of neuroleptic treatment during the index episode was 12 weeks ($SD=6.5$). Neuroleptic doses in chlorpromazine equivalents (12) ranged from 20 mg/day to 1660 mg/day, with a mean of 806 mg/day ($SD=461$). For the purpose of this study, chlorpromazine and thioridazine were considered low-potency neuroleptics and all other neuroleptics were classified as high potency. Anticholinergic drugs, usually benztropine mesylate, were used in 23 (38%) of the patients who received neuroleptics. Twenty (33%) of the 60 patients received combination treatment with lithium salts, antidepressants, or both. In the group of patients treated with psychotropic medication other than neuroleptics, 37 (79%) of the patients were receiving antidepressants, 15 (32%) lithium salts, five (11%) anticonvulsants, 12 (26%) benzodiazepines, and 22 (47%) a combination of these.

All patients were examined within the first 2 weeks of admission. One rater conducted structured interviews regarding sensory complaints subjectively attributed to the pharmacological treatment, and another rater examined patients for signs of parkinsonism and

akathisia. The two raters were blind to each other's findings and the medication status of patients. The structured interview regarding sensory complaints used a modified version of the McGill Pain Questionnaire (13; modified questionnaire available on request from P.D.). The McGill Pain Questionnaire is a structured interview that assesses the clinical features of painful states as well as the psychosocial context of subjects complaining of pain. For the purpose of this study, only the painful sensations specifically related by patients to the current pharmacological treatment were considered, and the interview was limited to those sections pertaining to the description of pain. In these sections, patients are asked to select from lists those words or subgroups of similar words best describing the frequency (e.g., continuous, steady, constant versus brief, momentary, transient), type (e.g., hot, burning, scalding versus cool, cold, freezing), and severity (on a 5-point scale on which mild=1 and 5=excruciating) of the painful sensations and to indicate with the help of body maps the localization of the pain, further specifying whether the sensations referred to the surface (i.e., skin) or inside the body (e.g., joint, muscle, bone). The section pertaining to the description of type of painful states was modified so that single words rather than groups of similar words were presented to the patients (e.g., burning rather than hot, burning, scalding). The questionnaire was also modified to include direct questions about complaints of heaviness and stiffness and about the possible coexistence of dystonic reactions with painful states. A similar revision of the McGill Pain Questionnaire was previously used in a study of pain in Parkinson's disease (1), and its clinical relevance for categorizing painful states in this condition has been demonstrated.

Subjective sensory complaints of heaviness and stiffness that likely were a result of rigidity or bradykinesia, or those associated with acute dystonic reactions, were not considered primary sensory symptoms. Primary sensory symptoms were recorded as either pain or paresthesias. In accord with neurological convention (1-4), burning sensations were considered paresthesias rather than pain. Four motor signs of parkinsonism (bradykinesia, rigidity, tremor, and postural instability) were rated on a standard 5-point scale (14) on which 0=absence of abnormal signs and 4=severe impairment, and the criterion for diagnosis of parkinsonism was a mean score of 1 on this scale. A combination of awareness of restlessness with characteristic restless movements such as rocking from foot to foot when standing defined akathisia (15).

Because of significant skewness in the distributions of age, pain intensity, and items representing parkinsonism, the data were analyzed by using nonparametric statistics. Specifically, bivariate comparisons were examined by using Spearman rank correlation coefficients, and between-group comparisons were examined by using Mann-Whitney tests. All values were corrected for ties. Chi-square tests with continuity correction were used to compare distributions of dichotomous

TABLE 1. Diagnoses of Psychiatric Patients Treated With Neuroleptic or Other Medications^a

Diagnosis	Patients Receiving Neuroleptics (N=60)		Patients Receiving Other Medications (N=47)	
	N	%	N	%
Schizophrenia	33	55	5	11
Nonpsychotic mood disorder	5	8	28	60
Psychotic mood disorder	19	32	2	4
Personality disorder	3	5	12	25

^aDifference among diagnostic groups was significant ($\chi^2=55.06$, $df=3$, $p<0.0001$).

variables and diagnostic categories. Two-tailed significance values were used throughout.

RESULTS

Patients Receiving Neuroleptics Versus Those Receiving Other Medications

The neuroleptic-treated group included 26 men and 34 women; the patients treated with medications other than neuroleptics included 19 men and 28 women ($\chi^2=0.01$, $df=1$, $p=0.92$). The mean age of the patients receiving neuroleptics was 31.4 years ($SD=10.1$); that of the patients treated with other medications was 35.5 years ($SD=12.2$) (Mann-Whitney $U=1177$, $p=0.14$). The diagnoses of the two groups of patients are presented in table 1. The two groups were demographically similar but differed significantly in their diagnostic composition. Not unexpectedly, more of the patients receiving neuroleptics had psychotic conditions, such as schizophrenic disorders and psychotic mood disorders, than did the patients receiving other medications.

Fourteen (23%) of the 60 patients receiving neuroleptics complained of pain, in contrast to only one (2%) of the 47 patients treated with nonneuroleptic medications ($\chi^2=8.2$, $df=1$, $p<0.005$). There was no difference between the groups in subjective complaints of paresthesias: five (8%) of the patients receiving neuroleptics versus four (9%) of the patients receiving other medications ($\chi^2=0.10$, $df=1$, $p=0.75$). Among the patients receiving neuroleptics, the pain was described as intermittent by 10 of the 14 subjects, and aching was the most common type of complaint ($N=12$). Twelve patients localized their pain to the four limbs, and five to the back; none localized their pain to the head or ventral torso. Depth localization was defined as poorly localized by 11 patients.

Patients Receiving Neuroleptics Who Did Versus Those Who Did Not Have Neuroleptic-Induced Extrapyrimal Syndrome

Twenty-two (37%) of the 60 patients receiving neuroleptics met study criteria for neuroleptic-induced extra-

TABLE 2. Characteristics of Patients Receiving Neuroleptics Who Did or Did Not Have Neuroleptic-Induced Extrapyrimal Syndrome

Item	Patients With Extrapyrimal Syndrome (N=22)		Patients Without Extrapyrimal Syndrome (N=38)		Analysis
	N	%	N	%	
Sex					$\chi^2=1.21$, $df=1$, $p=0.27$
Men					
N	7		19		
%	32		50		
Women					
N	15		19		
%	68		50		
Diagnosis					$\chi^2=3.34$, $df=2$, $p=0.18$
Schizophrenia					
N	9		24		
%	41		63		
Psychotic mood disorder					
N	10		9		
%	45		24		
Nonpsychotic disorder					
N	3		5		
%	14		13		
Age (years)					$U=354$, $p=0.33$
Mean	34.5		30.2		
SD	12.6		7.9		
Neuroleptic dose (chlorpromazine equivalents)					$U=330$, $p=0.17$
Mean	923		738		
SD	470		449		
High-potency neuroleptic					$\chi^2=0.22$, $df=1$, $p=0.64$
N	16		24		
%	73		63		
Anticholinergic treatment					$\chi^2=1.30$, $df=1$, $p=0.26$
N	11		12		
%	50		32		
Paresthesias					$\chi^2=0.42$, $df=1$, $p=0.52$
N	3		2		
%	14		5		
Pain					$\chi^2=16.26$, $df=1$, $p<0.001$
N	12		2		
%	55		5		
Pain intensity score					$U=212$, $p<0.0001$
Mean	2.0		0.2		
SD	2.0		0.9		

pyramidal syndromes. Of this group, 15 presented with parkinsonism, four with akathisia, and three with both. Demographic, clinical, and treatment characteristics of these patients did not significantly differ from those of patients classified as not having neuroleptic-induced extrapyramidal syndromes (table 2). Significantly more of the patients with neuroleptic-induced extrapyramidal syndromes complained of pain (table 2). In all 60 patients receiving neuroleptics, the reported intensity of pain was significantly correlated with the parkinsonism

TABLE 3. Characteristics of Patients Treated With Neuroleptics Who Did or Did Not Report Pain Symptoms

Item	Patients Not Reporting Pain (N=46)	Patients Reporting Pain (N=14)	Analysis
Sex			$\chi^2=0.12$, df=1, p=0.73
Men			
N	21	5	
%	46	36	
Women			
N	25	9	
%	54	64	
Diagnosis			$\chi^2=0.19$, df=2, p=0.91
Schizophrenia			
N	26	7	
%	57	50	
Psychotic mood disorder			
N	14	5	
%	30	36	
Nonpsychotic disorder			
N	6	2	
%	13	14	
Age (years)			U=279, p=0.45
Mean	31.1	34.1	
SD	9.3	12.2	
Neuroleptic dose (chlorpromazine equivalents)			U=316, p=0.92
Mean	805	811	
SD	468	457	
High-potency neuroleptic			$\chi^2=0.01$, df=1, p=0.91
N	30	10	
%	64	71	
Anticholinergic treatment			$\chi^2=0.01$, df=1, p=0.93
N	17	6	
%	37	43	
Akathisia			$\chi^2=0.68$, df=1, p=0.41
N	4	3	
%	9	21	
Parkinsonism			$\chi^2=8.20$, df=1, p=0.004
N	9	9	
%	20	65	
Parkinsonism rating			U=184, p=0.01
Mean	0.48	0.95	
SD	0.50	0.60	
Tremor rating			U=200, p=0.02
Mean	0.54	1.21	
SD	0.80	1.10	
Postural instability rating			U=267, p=0.05
Mean	0.04	0.21	
SD	0.20	0.40	
Rigidity of motor joints rating			U=219, p=0.05
Mean	0.67	1.21	
SD	0.90	1.00	
Bradykinesia rating			U=232, p=0.08
Mean	0.65	1.15	
SD	1.00	1.00	

severity score ($r=0.31$, $p<0.02$), and the pain intensity score was significantly higher among the patients with than those without neuroleptic-induced extrapyramidal syndromes (table 2).

The presence of pain was not related to sex, current age, neuroleptic dose, neuroleptic potency (high versus low), or anticholinergic drug use (table 3). When patients with akathisia alone were excluded from the analysis, subjective complaints of pain were noted in nine (50%) of the 18 patients with parkinsonism, in contrast to two (5%) of the 38 patients without parkinsonism ($\chi^2=12.8$, df=1, $p<0.001$). When patients with parkinsonism alone were excluded, subjective pain was noted in three (43%) of the seven patients with akathisia and in two (5%) of the 38 patients without akathisia ($\chi^2=5.1$, df=1, $p<0.05$). A forward stepwise regression analysis was conducted to determine which dimensions of neuroleptic-induced extrapyramidal syndromes (akathisia, bradykinesia, postural imbalance, rigidity of motor joints, and tremor) uniquely predicted the intensity of pain. Tremor ($F=7.1$, df=1, 58, $R^2=0.09$, $p<0.01$) and postural imbalance ($F=4.2$, df=1, 57, $R^2=0.06$, cumulative $R^2=0.15$, $p<0.05$) had significant predictive value, whereas associations were not statistically significant for the other variables ($F<1.5$ for all).

DISCUSSION

The main findings of this study were 1) patients receiving acute neuroleptic treatment exhibited more complaints of pain attributed directly to the medication than patients receiving psychotropic agents other than neuroleptics and 2) among the neuroleptic-treated group, complaints of pain were more frequent in patients with parkinsonism, akathisia, or both. The interpretation of these findings must be very cautious because the study is preliminary and has two major methodological limitations. First, data on complaints of pain were gathered in single interviews with a questionnaire that has not been standardized in psychiatric populations. Thus, the reliability of the findings is open to question. Undoubtedly, the absence of reliability data concerning the McGill Pain Questionnaire poses a major threat to the validity of the study and warns against any definitive interpretation of the results. Second, the cross-sectional design of the study leaves unanswered the question of whether pain is a direct adverse effect of neuroleptic treatment. Clearly, a prospective, longitudinal study in which complaints of pain are reliably measured before and during exposure to neuroleptics is more likely to adequately address this important question. The limitations notwithstanding, several clinically relevant observations were made.

The pain was usually described as a poorly localized, intermittent, aching sensation involving all four limbs symmetrically and sparing the head and ventral torso. This description of pain closely resembles that reported in the neurological literature on parkinsonism. Among patients receiving neuroleptics the intensity of reported

pain was significantly correlated with the severity of parkinsonism, and in univariate tests all components of the parkinsonian syndrome were rated higher in patients with pain than in those without pain. A stepwise regression analysis showed the relation between parkinsonism and pain to be mediated by tremor and postural balance rather than motor rigidity and bradykinesia. However, tremor, motor rigidity, and bradykinesia were highly intercorrelated, and chance may have emphasized the effect of one over the others. The finding could also have been influenced by our exclusion from consideration of complaints of heaviness and stiffness, which a priori were presumed to be secondary to rigidity and bradykinesia. By contrast, there was no relation between reported pain and akathisia in either univariate or multivariate analyses. Neither the presence nor the intensity of reported pain was related to age, sex, dose or potency of the neuroleptic, or adjunctive use of anticholinergic medications. In addition, reports of pain were almost equally distributed among psychiatric diagnoses, suggesting that patients did not report pain as a consequence of psychosis. However, the small number of patients (N=8) in the nonpsychotic group suggests caution in interpreting this finding, and we cannot rule out the possibility that at least some patients may have reported pain as a result of delusional or hallucinatory experiences.

To our knowledge, there have been no previous studies specifically examining sensory complaints associated with neuroleptic treatment. The report by Sigwald and Solignac (16) is the only notable exception to the general neglect of this issue. In a survey of sensory symptoms in 213 patients with parkinsonism, they commented on the similarities between the disagreeable or painful manifestations of Parkinson's disease and those associated with neuroleptic therapy. It is not entirely clear why there has been no follow-through on these original observations. In their evaluation of extrapyramidal side effects, patients and psychiatrists alike appear to have placed more clinical emphasis on the subjective emotional states engendered by neuroleptics than on sensory phenomena. If primary sensory phenomena associated with neuroleptics are mostly limited to pain, as the results of our study indicate, the fact that pain comprises both sensory and affective dimensions (17) and the difficulties in verbalizing adequately its sensory component may at least in part account for the lack of appreciation of sensory symptoms in the psychiatric literature.

Very soon after the introduction of neuroleptics into psychiatry, it was realized that "all the side effects of neuroleptics had already been described between 1920 and 1935 as a sequela of [Von Economo] encephalitis" (18). The spectrum of symptoms included specific mental states associated with certain motor disturbances, that is, bradyphrenia associated with bradykinesia and impatience associated with akathisia. Since then, it has been customary to classify broadly the neuroleptic-induced extrapyramidal symptoms as either purely motor disturbances (e.g., dystonia, tremor) or mixed motor

and mental disturbances (e.g., akathisia, bradykinesia). Some clinicians have emphasized the existence of dysphoric states induced by neuroleptics, that is, generalized feelings of unwellness, which cannot be fully explained by the severity of motor disorders or are not associated with motor manifestations (19-21). A main characteristic of this dysphoric response to the medication is a distinctly unpleasant, affective quality of mentation associated with somatic complaints that often are vaguely expressed as "just not feeling right." Occasionally this response is described vividly as peculiar sensations, like the patient described by Van Putten and May (20) who complained that neuroleptic treatment had induced a "hangover without headache." We hypothesize that at least some of these dysphoric states may be sustained by unpleasant sensory phenomena.

The pathogenesis of primary sensory symptoms in parkinsonism is poorly understood. Given the general absence of gross lesions in the peripheral nervous system and central sensory pathways, several authors have suggested that these symptoms may be another manifestation of central dopaminergic deficiency relating to dysfunction of basal ganglia (2, 4, 22). There is some evidence that the basal ganglia somehow modify sensory perception, and electrophysiological studies indicate that striatal influences on sensory activity are mainly inhibitory (23). Snider et al. (4) speculated that spontaneous sensory symptoms could be related to release of sensory centers from extrapyramidal influence. Alternatively, Nutt and Carter (6) pointed out how the descending dopaminergic tracts projecting to both dorsal horn and midline thalamic nuclei (24, 25) provide an anatomical substrate for dopaminergic influence on sensory input and perception. Although the findings of our study do not substantially contribute to elucidating the pathogenesis of sensory symptoms, they are consistent with the view that reduced dopaminergic transmission by itself, in the absence of neuropathological lesions, may be a sufficient factor in the genesis of such symptoms.

In conclusion, it must be reiterated that although the results of this study are consonant with the hypothesis that neuroleptic treatment is associated with pain, their validity may be questionable. Until these findings are replicated in subsequent studies using psychometrically standard methods, no definitive conclusions can be reached.

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Prevalence of Tardive Dyskinesia, Tardive Dystonia, and Respiratory Dyskinesia Among Chinese Psychiatric Patients in Hong Kong

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Objective: Only scanty information on the prevalence of tardive dyskinesia in Chinese patients has been available. This study was undertaken to examine the prevalence of tardive dyskinesia, tardive dystonia, and respiratory dyskinesia in Chinese psychiatric patients in Hong Kong. **Method:** All inpatients of a mental hospital in Hong Kong, except those in the admission and children's wards, were surveyed with the Abnormal Involuntary Movement Scale, and standard research criteria were used to establish the diagnosis of tardive dyskinesia. In addition, patients were screened for tardive dystonia, according to published criteria, and for respiratory dyskinesia by physical examination and laboratory tests. **Results:** Among the 917 patients surveyed, the prevalence rates were 9.3% for tardive dyskinesia, 0.4% for tardive dystonia, and 1.2% for respiratory dyskinesia. With multivariate analysis, greater age and a lower current dose of antipsychotic, but not the presence of mood disorder, were factors found to be significantly associated with tardive dyskinesia. **Conclusions:** The prevalence rates were much lower than those found in Western studies. This may indicate that there is an ethnic difference in the prevalence of these conditions. Prospective cross-cultural studies are necessary to explore this possibility.

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Tardive dyskinesia is an involuntary movement disorder associated with prolonged use of neuroleptics. Kane and Smith (1) reviewed 56 studies involving 34,555 patients and found an average prevalence of 20%. In the same article, these investigators reviewed 19 studies on spontaneous dyskinesia and identified a prevalence of 5%. These were mostly American and European studies; information on Chinese patients is scanty.

Eleven Asian studies on the prevalence of tardive dyskinesia, involving 8,647 patients, have so far been published (2-12). The average prevalence is 11.6%, but the range is wide (2.5%-27.6%). This variability is multifactorial and may be due to differences in the methods of assessing dyskinesia, to sociodemographic and clinical characteristics, and/or to the fluctuating nature of tardive dyskinesia. In fact, earlier studies were fraught with methodological problems, such as use of variable

diagnostic criteria, methods of case finding, and examination techniques. In the three studies that examined a homogeneous population of Chinese patients, the Taipei study (3) did not provide details on diagnosis and methodology, the Hong Kong study (6) did not use a standardized instrument to assess dyskinesia, and the Shanghai study (10) involved only chronic schizophrenic patients.

Our first aim, therefore, was to examine the prevalence of tardive dyskinesia in various groups of Chinese psychiatric patients by using an improved method. In addition, we wished to examine the prevalence of tardive dystonia and respiratory dyskinesia. Tardive dystonia (13) is an underrecognized condition that is frequently more disabling than classical tardive dyskinesia. Although it may be a variant or subsyndrome of tardive dyskinesia, it is potentially useful to isolate it in epidemiological and treatment studies, since there is preliminary evidence that it differs from classical tardive dyskinesia in some significant ways (14). In this article, the term "tardive dyskinesia" is therefore confined to the bucco-linguo-masticatory syndrome and choreoathetoid movements of the limbs and trunk. Respiratory dyskinesia is characterized by irregularity in the rate, rhythm, and depth of breathing and usually occurs in patients with tardive dyskinesia (15).

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TABLE 1. Prevalence of Tardive Dyskinesia and Data on Drug Treatment of 917 Chinese Psychiatric Patients in Hong Kong

Diagnosis	Patients With Tardive Dyskinesia (N=85)		Patients Currently Taking Antipsychotic Drugs (N=792)		Current Dose of Antipsychotic (mg/day of chlorpromazine equivalents)		Patients Currently Taking Anticholinergic Drug (N=563) ^a	
	N	%	N	%	Mean	SD	N	%
Schizophrenia (N=602)	51	8.5	589	97.8	993.4	881.8	452	76.7
Manic-depressive psychosis, circular type (N=22)	4	18.2	15	68.2	710.0	1044.3	12	80.0
Manic-depressive psychosis, depressed type (N=22)	5	22.7	6	27.3	48.9	121.1	3	50.0
Dementia (N=97)	14	14.4	54	55.7	77.0	222.6	10	18.5
Mental retardation (N=97)	3	3.1	79	81.4	529.9	617.1	57	72.2
Other (N=77)	8	10.4	49	63.6	255.9	385.2	29	59.2

^aRefers to patients currently taking antipsychotic drugs.

METHOD

Our survey was conducted from October to November 1989 in one of the three mental hospitals in Hong Kong. At the outset of the study, 30 randomly chosen patients were examined independently by two of the investigators (H.C. and L.L.), both psychiatrists, with the Abnormal Involuntary Movement Scale (AIMS) (16) to test interrater reliability. Kappas for the seven items of the AIMS ranged from 0.8 to 1.0.

All inpatients except those in the admission and children's wards were examined by one or the other of the two investigators (H.C. and L.L.) with the AIMS after informed consent had been given. Patients in the admission wards were excluded because they were mentally unstable and their clinical diagnoses were frequently uncertain. Clinical diagnoses had been made previously according to ICD-9 by the psychiatrists in charge of the patients. The investigators were blind to these diagnoses.

Schooler and Kane's research diagnostic criteria (17) were used to establish the diagnosis of tardive dyskinesia. Prerequisites include 1) exposure to antipsychotics for at least 3 months, 2) at least "mild" involuntary movements in two or more body areas or at least "moderate" involuntary movements in one or more body areas, and 3) absence of other conditions causing involuntary movement.

All patients were also examined for the presence of tardive dystonia according to the criteria of Burke et al. (13): 1) the presence of chronic dystonia, 2) history of antipsychotic drug treatment preceding or concurrent with the onset of dystonia, 3) exclusion of known causes of secondary dystonia by appropriate clinical and laboratory evaluation, and 4) no family history of dystonia. To exclude secondary causes of dystonia, affected subjects underwent further examination, including CBC, tests of liver, renal, and thyroid function, determination of ceruloplasmin and copper levels, and slitlamp examination.

In the examination for respiratory dyskinesia, patients were bared to the waist and respiration was observed for 3 minutes in both sitting and lying positions. Irregularity of breathing rate, rhythm, and depth was necessary for the diagnosis. Using such criteria, we

found that the presence or absence of respiratory dyskinesia was determined without difficulty. Affected patients were also examined for cardiac or lung disease and underwent a battery of tests, including ECG, chest X-ray, determination of serum electrolyte levels, liver function, and blood gases, and CBC. Polygraphic recordings of thoracic and abdominal respiratory efforts were performed to confirm the dyskinesia objectively.

All patients were subsequently interviewed. In addition, case notes and drug charts were reviewed for demographic data and family, psychiatric, and treatment histories.

Patients with tardive dyskinesia were reexamined with the AIMS 3 months after their initial interviews. Those who continued to meet the criteria for tardive dyskinesia were diagnosed as having persistent tardive dyskinesia (17).

The 95% confidence intervals of prevalence were calculated for the different diagnostic subgroups. Both univariate (Mann-Whitney test and chi-square test) and multivariate (logistic regression) analyses were used to identify the factors associated with tardive dyskinesia.

RESULTS

Nine hundred seventeen patients (503 male and 414 female) were surveyed, among whom 863 (94.1%) had histories of exposure to antipsychotic medication. Their mean age was 46.5 years (SD=18.0, range=16-103), and the mean duration of hospitalization was 3.1 years (SD=2.4). Seven hundred ninety-two (86.4%) of the patients were currently taking antipsychotic drugs (table 1). Their mean current dose of antipsychotic in chlorpromazine equivalents (18) was 876.3 mg/day (SD=853.1, median=600, range=10-4725). Patients were commonly prescribed one to three types of antipsychotic drugs; chlorpromazine was the most widely used, followed by trifluoperazine, haloperidol, and thioridazine (table 2). Of the 792 patients currently taking antipsychotics, 71.1% were given an anticholinergic drug (table 1). Trihexyphenidyl was the only anticholinergic drug used, and the mean daily dose was 6.29 mg (SD=3.02).

TABLE 2. Patients Currently Taking the Four Most Commonly Prescribed Antipsychotic Drugs in a Survey of 917 Chinese Psychiatric Patients in Hong Kong

Diagnosis	Patients Taking Chlorpromazine (N=336)		Patients Taking Trifluoperazine (N=221)		Patients Taking Haloperidol (N=195)		Patients Taking Thioridazine (N=145)	
	N	%	N	%	N	%	N	%
Schizophrenia	267	79.5	197	89.1	136	69.7	94	64.8
Manic-depressive psychosis, circular type	4	1.2	1	0.5	10	5.1	3	2.1
Manic-depressive psychosis, depressed type	3	0.9	2	0.9	0	0.0	2	1.4
Dementia	13	3.9	3	1.4	11	5.6	28	19.3
Mental retardation	35	10.4	9	4.1	23	11.8	5	3.4
Other	14	4.2	9	4.1	15	7.7	13	9.0

Eighty-five patients had tardive dyskinesia (table 1), a prevalence of 9.3% (95% confidence interval=7.4%–11.2%). The mean age of these patients was 61.7 years (SD=15.9, range=24–94). Seventy-two (84.7%) of these patients had persistent tardive dyskinesia. No patients without a history of exposure to antipsychotics had dyskinesia.

The majority of the patients (N=602) were schizophrenic (table 1), among whom the prevalence of tardive dyskinesia was 8.5% (9.5% confidence interval=6.3%–10.7%).

Four patients (two of each sex) had tardive dystonia, a prevalence of 0.4% (95% confidence interval=0.1%–1.1%). Their mean age was 39.3 years (SD=1.1, range=38–41). The duration of dystonia ranged from 2 to 5 years. Two of these patients had coexistent tardive dyskinesia.

Eleven patients (three male and eight female) had respiratory dyskinesia, an overall prevalence of 1.2% (95% confidence interval=0.6%–2.2%) and a prevalence of 12.9% among those with tardive dyskinesia. Their mean age was 65.5 years (SD=16.0, range=38–89). Clinical and polygraphic characteristics of these patients will be presented in a separate paper.

Older age (Mann-Whitney test, $z=-7.9$, $p<0.0001$), female sex ($\chi^2=8.34$, $df=1$, $p=0.004$), lower current dose of antipsychotic (Mann-Whitney test, $z=-6.7$, $p<0.0001$), and a diagnosis of manic-depressive psychosis ($\chi^2=14.86$, $df=1$, $p=0.01$) were individually associated with a higher risk of tardive dyskinesia. Among schizophrenic patients, duration of mental illness was not significant.

Table 3 shows the logistic regression analysis of the significant variables. Schizophrenia was used as the reference for the category of diagnosis. Older age and a lower current dose of antipsychotic were still significantly associated with a higher risk of tardive dyskinesia, but sex lost its significance. Dementia and "other" diagnoses were associated with a lower risk of tardive dyskinesia.

DISCUSSION

We found a relatively low prevalence of tardive dyskinesia (9.3%) among Chinese psychiatric patients in Hong Kong. The prevalence of 8.5% among the schizo-

TABLE 3. Summary of Multivariate Logistic Regression Analysis to Predict Risk of Tardive Dyskinesia in a Survey of 917 Psychiatric Patients in Hong Kong^a

Independent Variable	Coefficient: b_i	Standard Error: $s(b_i)$	F ^b	p
Age	0.04519	0.0093	26.1	<0.01
Sex	-0.18956	0.2640	0.6	0.45
Current antipsychotic dose	-0.00133	0.0003	16.3	<0.01
Diagnosis ^c				
Manic depressive psychosis, circular type	-0.20758	0.6325	0.1	0.73
Manic depressive psychosis, depressed type	-0.60833	0.5685	1.3	0.26
Dementia	-1.44160	0.3978	14.6	<0.01
Mental retardation	-0.75919	0.6428	1.6	0.21
Other	-0.86089	0.4409	4.2	0.04
Constant	-3.60570	0.6333	36.0	<0.01

^aModel $\chi^2=95.1$, $df=8$, $p<0.0001$; goodness-of-fit $\chi^2=427.6$, $df=813$, $p=1.00$.

^bF-to-remove statistic: $F=b_i/s(b_i)^2$; $df=1$, 879. F statistic tests whether the reduced model with the relevant variable removed is statistically different from the original model.

^cSchizophrenia was used as the reference diagnosis.

phrenic patients is remarkably similar to the 8.4% among chronic schizophrenic patients in Shanghai (10). This low prevalence is also similar to the average prevalence of 11.6% in other Asian studies (2–12). The Shanghai (10) and Indian (5) investigators attributed the low prevalence of tardive dyskinesia to the low dosage of antipsychotic used. In our study, the mean current dose of antipsychotic was 876.3 mg/day (SD=853.1) of chlorpromazine equivalents. This is at least comparable to the dosage commonly used in Western countries, even without adjusting for the generally lower body weight of the Chinese.

The reasons for our finding of a lower prevalence of tardive dyskinesia than that in Western studies are at present unclear. Recently, Tan and Tay (12) found in Singapore that the prevalence of tardive dyskinesia in Eurasians was higher than in Asians; they speculated that genetic differences in sensitivity to antipsychotics might be responsible. This possibility needs to be explored further in prospective cross-cultural studies.

An unexplored area in our survey is the effect of drug-induced parkinsonism on tardive dyskinesia. Although not unanimously confirmed, an inverse relation be-

tween tardive dyskinesia and drug-induced parkinsonism was previously reported and was attributed to a masking bradykinetic effect of parkinsonism on tardive dyskinesia (19, 20). The high frequency of use of anticholinergic drugs (71.1%) and the high mean current dose of antipsychotic in our survey indicate that drug-induced parkinsonism was common among our subjects and therefore makes this possible interaction particularly relevant to our study. Unfortunately, we did not assess drug-induced parkinsonism, and the possibility that suppression of tardive dyskinesia by drug-induced parkinsonism may have been responsible for the low prevalence of tardive dyskinesia needs to be explored in future studies.

The association of old age with a higher risk of tardive dyskinesia is expected (21). The association of a lower current dose of antipsychotic with a higher risk of tardive dyskinesia has also been reported (11). This may be due to the suppressing effect of a higher dose of antipsychotic on tardive dyskinesia and/or doctors' attempts to reduce antipsychotic dosage after tardive dyskinesia was detected.

Mood disorder was found to be associated with a higher risk of tardive dyskinesia in some studies that did not use multivariate analysis (22, 23). We failed to confirm this. Similarly, although organic brain damage has been reported to be a risk factor for tardive dyskinesia (24), in our study dementia was associated with a lower risk of tardive dyskinesia after we adjusted for age and current dose of antipsychotic.

So far, two small studies on tardive dystonia (25, 26) have found a prevalence of 1.5%–2%. If tardive dystonia is a subsyndrome of tardive dyskinesia (14), our finding of 0.4% is consistent with the lower prevalence of tardive dyskinesia in our patients. The mean age at onset of tardive dystonia in our group was 36.4 years, but the small number of patients precludes any firm conclusion about a younger age at onset of tardive dystonia (13, 25) than at onset of tardive dyskinesia. Of the four patients affected, "bizarre posture" and "histrionic look" were the only comments recorded in the case notes of three of them. This lends support to the idea that this still controversial condition is underrecognized (13).

There have been two previous studies on the prevalence of respiratory irregularity in chronic mental patients (27, 28). Yassa and Lal (27) found a prevalence of 2.3% in 351 chronic inpatients and a prevalence of 7.4% among those with tardive dyskinesia (ages unknown). In contrast, Youssef and Waddington (28) reported the high prevalence of 45% among 76 patients who suffered from schizophrenia, bipolar disorder, and mental handicap in addition to tardive dyskinesia. Since respiratory dyskinesia is probably more common in the elderly, the relatively old age (mean=63.6 years) of their sample might have inflated the prevalence rate. Our finding of 1.2% is a low figure.

One obvious limitation of our study is its cross-sectional design, which precludes accurate judgment about risk factors and causal relationships. Prospective cross-

cultural studies, albeit difficult and costly, are needed in the future. The second limitation is the lack of information on the cumulative antipsychotic dose, which is virtually impossible to obtain in our local setting. Instead, the current daily dose of antipsychotic was used, and this has a rather different implication. Third, the clinical diagnoses were made by the psychiatrists in charge of the patients according to ICD-9, which did not provide standard diagnostic criteria. It therefore remains possible that there were misdiagnoses, especially confusion between schizophrenia and manic-depressive psychosis (29), for some of the survey patients. While this may have led to an inaccurate representation of patients in the various diagnostic categories, it should not have affected the overall prevalence of tardive dyskinesia found in our study.

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CSF β -Endorphin and Dynorphin in Bulimia Nervosa

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Objective: Preclinical and clinical evidence suggests that central opioid dysfunction may play a role in the pathophysiology of the eating disorders. In particular, endogenous opioids are known to regulate feeding behavior, mood, perception, and neuroendocrine function, all of which are disturbed in patients with eating disorders. Although low concentrations of CSF β -endorphin have been reported in low-weight patients with anorexia nervosa, central opioid activity in normal-weight patients with bulimia nervosa has not been reported. The authors therefore measured CSF concentrations of β -endorphin and dynorphin in drug-free female patients with DSM-III-R-defined bulimia nervosa and normal comparison subjects. **Method:** After 4 days of a low monoamine diet and overnight bed rest, CSF was obtained (12–26 cc) from 11 women with bulimia and 17 normal comparison subjects (eight women and nine men). **Results:** The women with bulimia had significantly lower CSF concentrations of β -endorphin than did the female comparison subjects. However, CSF concentrations of dynorphin were not significantly different in patients and female or male comparison subjects. β -Endorphin concentrations were inversely correlated with Beck Depression Inventory scores and the depression subscale of the Eating Disorders Inventory. **Conclusions:** These data support a role for central opiates in the mediation of the pathophysiology of the signs and symptoms of bulimia nervosa, although it is impossible to rule out the effects of depression on the results. (Am J Psychiatry 1992; 149:1086–1090)

Preclinical and clinical evidence suggests that alterations in endogenous opioid function are associated with alterations in feeding (1–8), mood (8, 9), perception (8, 10), and neuroendocrine function (11), all of which are characteristic of patients with eating disorders. In animals, opioid agonists increase and opioid antagonists decrease food intake. These effects appear to be mediated by several receptor types, including κ , μ , δ , and σ receptors (12, 13). A disturbance of opioid function could also contribute to the hypercortisolism observed in anorexia nervosa (14, 15). Kaye and associates found that underweight patients with anorexia nervosa had significantly lower CSF β -endorphin concentrations than healthy volunteers (16). These low CSF β -endorphin concentrations normalized after weight restoration. Lower concentrations of plasma β -endorphin have been reported in normal-weight pa-

tients with bulimia nervosa (17, 18). However, it is highly questionable whether plasma β -endorphin reflects central β -endorphin function. CSF levels of β -endorphin, as well as of dynorphin, have not been reported in normal-weight patients with bulimia nervosa. We therefore studied CSF levels of β -endorphin and dynorphin in a group of normal-weight patients with bulimia nervosa and healthy comparison subjects.

METHOD

Patients and comparison subjects were recruited through local newspaper advertisements and then interviewed with the Structured Clinical Interview for DSM-III (19), which was modified for DSM-III-R diagnosis. Patients with bulimia nervosa were included if they had experienced binge eating and purging at least three or more times per week for at least 6 months before the study. The mean weekly binge frequency was 8.2 times (SD=5.2) (range=3–19), and the mean weekly vomiting frequency was 4.7 times (SD=6.4) (range=0–19). Five patients had concurrent DSM-III-R-defined major depression, and six did not. Comparison subjects were ex-

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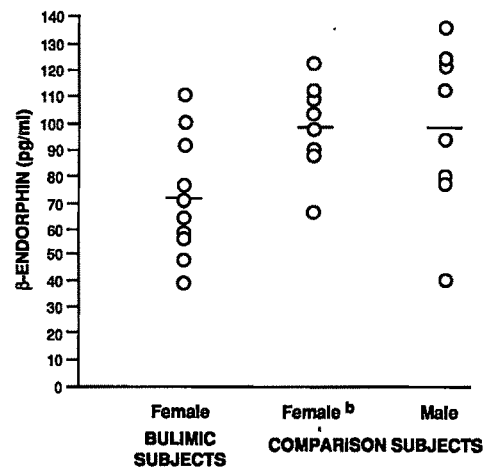
cluded if they had a lifetime or family history (first-degree relatives) of any major psychiatric illness. In addition, all comparison subjects were free of significant medical illnesses on the basis of a physical examination and routine laboratory tests. The study subjects consisted of 11 bulimic women and 17 normal comparison subjects (eight women and nine men). The mean age was 30.2 years (SD=6.4) for the women with bulimia, 35.5 years (SD=7.6) for the female comparison subjects (n.s.), and 26.7 years (SD=3.9) for the male comparison subjects (n.s.). Mean percent of average body weight was 102.6% (SD=13.1%) for the women with bulimia, 111.8% (SD=22.4%) for the female comparison subjects (n.s.), and 113.0% (SD=16.0%) for the male comparison subjects (n.s.); standardized weight tables were used (20).

All subjects were medication free for at least 4 weeks before the study. In addition, all subjects had a low monoamine diet for 4 days before CSF samples were obtained. Outpatient subjects were admitted to a clinical research unit on the night before the study. All subjects fasted after midnight, were kept at bed rest for 9 hours, and were allowed up only to go to the bathroom. Lumbar punctures were performed between 8:00 a.m. and 9:00 a.m., with subjects in the lateral decubitus position. CSF samples were immediately placed on wet ice, aliquoted, and frozen at -70°C . Samples were assayed in duplicate for β -endorphin₁₋₃₁ and dynorphin A₁₋₈ by radioimmunoassay (21, 22). Samples were diluted with radioimmunoassay buffer (pH=7.4, 0.02 M phosphate buffer containing 0.15 N NaCl, 0.1% bovine serum albumin, 0.01% thimerosal, and 0.1% triton-X-100) and were incubated overnight (18–24 hours) at 4°C with antiserum and ^{125}I -labeled tracers specific for dynorphin A₁₋₈ or β -endorphin₁₋₃₁. Free and bound tracers were separated by the addition of a 3% charcoal slurry and subsequent centrifugation ($2,500 \times g$ for 10 minutes at 4°C). The antiserum for dynorphin A₁₋₈ has 0.02% and 0.01% cross-reactivities for dynorphin A₁₋₁₃ and dynorphin A₁₋₁₇ and does not cross-react with met-enkephalin or leu-enkephalin. The sensitivity of this assay was 5 fmol/ml. The antiserum for β -endorphin₁₋₃₁ has 50% cross-reactivity with β -lipotropin and no cross-reactivity with met-enkephalin or α - or γ -endorphin. The sensitivity of this assay was 50 pg/ml.

Before the procedure, one of the investigators administered the Hamilton Rating Scale for Depression (23) and the Hamilton Rating Scale for Anxiety (24). In addition, subjects completed a series of psychological rating scales, including the Eating Disorders Inventory (25), the Eating Attitudes Test (26), the Beck Depression Inventory (27), and the Symptom Distress Checklist (SCL-90-R) (28) before lumbar puncture.

Statistical analysis was carried out by using the Statistical Analysis System (29). Between-group comparisons were performed with analysis of variance (ANOVA) and Student's *t* test. Correlations were determined with Spearman's rank order correlation (r_s) and were then corrected for number of comparisons.

FIGURE 1. CSF Levels of β -Endorphin in 10 Bulimic Women and Eight Female and Eight Male Comparison Subjects^a



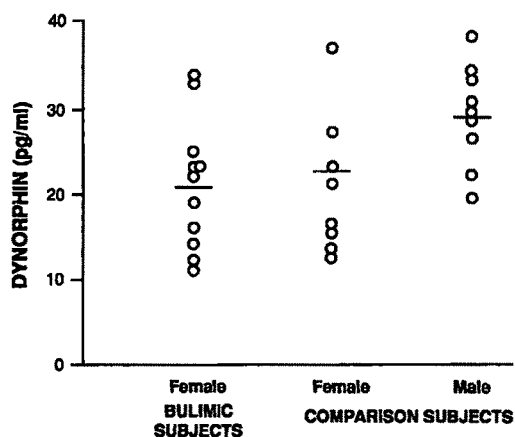
^aLevels of one bulimic woman and one male comparison subject were below the detectable limits of the assay (5 pg/ml) and were not included in the analysis. Horizontal lines represent means. Significant differences in CSF levels of β -endorphin were found among the three groups ($F=4.39$, $df=2, 24$, $p \leq 0.03$, ANOVA).

^bPost hoc differences persisted between bulimic women and female comparison subjects ($p \leq 0.05$, Bonferroni *t* test).

RESULTS

There was a significant difference in the CSF levels of β -endorphin between female patients with bulimia nervosa (mean=71.9 pg/ml, SD=23.0), female comparison subjects (mean=98.0 pg/ml, SD=17.7) ($p \leq 0.02$, unpaired *t* test), and male comparison subjects (mean=99.3 pg/ml, SD=19.3) ($p \leq 0.03$, ANOVA) (figure 1). (The β -endorphin levels of one bulimic patient and one male comparison subject were below the detectable limits of the assay [5 pg/ml] and were not included in this analysis.) After post hoc corrections, significant differences persisted between women with bulimia and female comparison subjects ($p \leq 0.05$, Bonferroni *t* test). There was a trend for differences in the CSF levels of dynorphin among women with bulimia (mean=21.3 pg/ml, SD=7.8), female comparison subjects (mean=22.7 pg/ml, SD=8.3), and male comparison subjects (mean=28.8 pg/ml, SD=6.0) ($p \leq 0.09$, ANOVA) (figure 2). However, there were no significant post hoc differences. CSF levels of β -endorphin and dynorphin were not significantly correlated to age or percent of average body weight in any of the groups or in the total cohort.

CSF levels of β -endorphin and dynorphin were correlated with several behavioral rating scales. CSF β -endorphin levels were significantly correlated with the Beck Depression Inventory ($p=0.0009$) (figure 3), the depression subscale score of the Eating Disorders Inventory ($p=0.001$) (figure 3), and the anger/hostility subscale of the SCL-90-R ($N=10$, $r_s=0.65$, $p=0.04$). There was a trend for CSF β -endorphin to be correlated

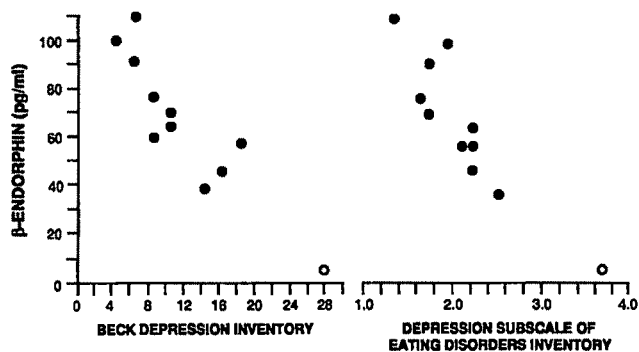
FIGURE 2. CSF Levels of Dynorphin in 11 Bulimic Women and Eight Female and Nine Male Comparison Subjects^a

^aHorizontal lines represent means. There was a trend for differences in CSF levels of dynorphin among bulimic women and female and male comparison subjects ($F=2.74$, $df=2, 25$, $p<0.09$, ANOVA).

with the Hamilton anxiety scale ($N=10$, $r_s=-0.62$, $p=0.06$). After Bonferroni corrections for the number of comparisons made, only the correlations between CSF β -endorphin levels and the two ratings of depression (Beck Depression Inventory and subscale score of the Eating Disorders Inventory) remained significant ($p\leq 0.02$). It should be noted that figure 3 includes an open circle that represents one bulimic subject whose β -endorphin levels were below the detectable limit of the assay (5 pg/ml), and although data on this patient were *not* included in the statistical analysis, they do support the relationship between low β -endorphin levels and high levels of depression.

CSF dynorphin concentrations were inversely correlated with weekly binge frequency ($N=11$, $r_s=-0.64$, $p=0.03$), Eating Attitudes Test scores ($N=11$, $r_s=-0.61$, $p=0.006$), and the thin subscale scores of the Eating Disorders Inventory ($N=11$, $r_s=-0.65$, $p=0.03$). There were trends for CSF dynorphin levels to be correlated with the interpersonal distrust subscale scores of the Eating Disorders Inventory ($N=11$, $r_s=0.55$, $p<0.1$) and the maturity fear subscale scores of the Eating Disorders Inventory ($N=11$, $r_s=-0.60$, $p=0.07$). However, none of these correlations involving CSF dynorphin levels remained significant after Bonferroni corrections.

Given the relationship with depression noted earlier, we compared CSF opiate levels in bulimic patients with and without concurrent major depression. There was a trend for depressed patients to have lower CSF β -endorphin concentrations ($N=4$, mean=55.6 pg/ml, $SD=16.5$) than nondepressed patients ($N=6$, mean=82.7 pg/ml, $SD=20.8$) ($t=2.18$, $df=8$, $p<0.07$). There was not a significant difference in CSF dynorphin concentrations between depressed ($N=5$, mean=17.2 pg/ml, $SD=6.5$) and nondepressed ($N=6$, mean=24.7 pg/ml, $SD=7.6$) women with bulimia nervosa ($t=1.76$, $df=9$, $p=0.11$).

FIGURE 3. Correlation Between CSF β -Endorphin Levels and Depression Scores in 10 Bulimic Women^a

^aCSF β -endorphin levels were significantly correlated with Beck Depression Inventory scores ($r_s=-0.87$, $p=0.0009$) and the depression subscale score of the Eating Disorders Inventory ($r_s=-0.87$, $p=0.001$). The open circle represents one subject whose β -endorphin levels were below the detectable limits of the assay (5 pg/ml) and is not included in this analysis.

DISCUSSION

This is the first report of lower CSF β -endorphin concentrations in normal-weight patients with bulimia nervosa than in female age-related comparison subjects. However, CSF dynorphin concentrations were not significantly different among groups. Our results are similar to the results reported by Kaye and colleagues, who found that CSF concentrations of β -endorphin and other peptides were low in patients with anorexia nervosa (16). However, the levels normalized after long-term stabilization of feeding and weight. The weights of our patients were not significantly different from those of their healthy comparison counterparts, and neither β -endorphin nor dynorphin concentrations in CSF were significantly correlated with percent of average body weight in any of the groups. Nevertheless, it is likely that our patient population, like that of others (30–32), had some degree of chronic semistarvation or malnutrition as a result of intermittent restriction of food intake. Although it was not statistically significant because of the large degree of variance, the fact that the weight of the bulimic patients was 9.2% of average body weight less than that of the comparison subjects may be clinically significant. Evidence suggests that patients with bulimia nervosa may have a higher set point for weight maintenance and could therefore be mildly underweight relative to their own “ideal” body weight (which is usually above the population weight) (33). This could conceivably result in low β -endorphin concentrations, possibly as a result of low levels of estrogen, which has been shown in animals to be necessary for the release of hypothalamic β -endorphin (34). In addition, acute food deprivation in rats results in elevations of pituitary β -endorphin immunoreactivity but not dynorphin content (35). Furthermore, binge eating and vomiting are likely to

result in secretion of corticotropin-releasing hormone (CRH), since plasma cortisol has been reported to increase after these behaviors (36) and to remain elevated (37). Unfortunately, plasma cortisol levels are not available from our group for comparison. One possible interpretation of these data may be that the stress of binge eating and purging leads to the release of CRH and the stimulation of the hypothalamic-pituitary-adrenal axis, including the pro-opiomelanocortin molecule from which β -endorphin is cleaved. Subsequent peptide depletion and/or opiate receptor down-regulation because of chronic binge eating, purging, and/or semistarvation may result in decreased CSF β -endorphin over time. This hypothesis is compatible with recent findings of reduced pain sensitivity in patients with eating disorders (38).

CSF levels of β -endorphin were highly correlated with two depression scales, and there was a trend for depressed women with bulimia to have lower levels than non-depressed patients. The reason for the lack of correlation with the Hamilton depression scale is unclear, but it may relate to less patient self-disclosure in an interview situation. It is impossible to say definitely whether the lower CSF concentrations of β -endorphin are due to depression or bulimia or an interaction between the two. A group of depressed nonbulimic patients was not available for comparison. However, other investigators have found no differences in β -endorphin or β -endorphin immunoreactivity between depressed patients and normal (39–41) or neurological (42) comparison subjects. In addition, no relationship between major depression and CSF β -endorphin levels was found in a group of patients with low back pain (43). Lower CSF β -endorphin levels have been reported in patients with alcohol dependence (44) and severe migraine (45), both of which may be related to bulimia (46, 47). Further studies of the relationship between CSF β -endorphin concentrations and depression are warranted.

Our findings also suggest that alterations of central opioid function may contribute to alterations in perception and behavior in patients with bulimia nervosa. Although levels of dynorphin were initially inversely correlated with weekly binge frequency, Eating Attitudes Test scores, and several subscale scores of the Eating Disorders Inventory, these correlations disappeared after correction for the large number of correlations performed. Nevertheless, this leaves open the possibility that dynorphin may be involved in an array of disturbances related to eating disorder pathology including binge eating, compulsivity, and body image distortion (10, 48, 49). Dynorphin is reported to play a major role in the modulation of the effects of other opiates and can have opposite effects on analgesia and temperature, as well as motor, cardiovascular, and respiratory effects, depending on the baseline state of the organism (48).

Research conducted in the field during the past two decades has clearly demonstrated that food intake is controlled by multiple neurotransmitters in the brain that are responsive to a complex array of metabolic, hormonal, and neural signals. Peptides have an important function in feeding, in part through their interac-

tion with monoamines (5, 50–52). It is also clear from studies of patients with eating disorders that several neuroregulatory systems are disturbed (53–55). It is therefore imperative that the available data be integrated into a comprehensive theory encompassing all involved systems, including the opiate system, if these findings are confirmed.

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A Monozygotic Mirror-Image Twin Pair With Discordant Psychiatric Illnesses: A Neuropsychiatric and Neurodevelopmental Evaluation

James B. Lohr, M.D., and H. Stefan Bracha, M.D.

One piece of genetic evidence for the biological distinctness of schizophrenia and bipolar illness is the rarity of monozygotic twin pairs in which one twin suffers from schizophrenia and the other from bipolar disorder. The authors describe a pair of monozygotic mirror-image twins with discordant diagnoses, schizophrenia in one twin and bipolar or schizoaffective disorder in the other.

(Am J Psychiatry 1992; 149:1091-1095)

Since Kraepelin first clearly divided the major mental illnesses into the broad categories of "dementia praecox" and "manic-depressive illness," researchers have puzzled over the relationship of these two conditions. Until 1982 there were no reports of twin pairs in which one twin suffered from schizophrenia and the other from bipolar disorder (1). In 1982 McGuffin et al. (2) reported identical male triplets, two of whom were diagnosed as having schizophrenia and the third of whom had bipolar illness. More recently, Dalby et al. (3) reported identical male twins, one of whom was reliably diagnosed as having schizophrenia and the other of whom had a diagnosis of mania. Studies of monozygotic twins have revealed very few pairs discor-

dant for schizophrenia and bipolar disorder, which supports the biological distinctness of schizophrenia and bipolar illness. Most of the other available genetic evidence also supports the distinctness of the two conditions (1, 4, 5), although there is some disagreement (6, 7).

The present paper is a neuropsychiatric study of one pair of monozygotic twins who appear to be discordant for schizophrenia and either bipolar illness or schizoaffective disorder. An interesting and unusual feature of these twins is that they are mirror images of one another.

CASE REPORTS

Both twins received physical examinations, CT scans, EEGs, and medical workups including thyroid function tests, CBC, electrolyte measurements, and urinalysis. All the results were within normal limits. Apart from a brief history of mild cannabis abuse, there was no history of substance abuse in either twin and no other evidence that the mental disorder was secondary to organic factors. Their prenatal and birth histories were unremarkable. There was no known family history of major mental illness.

Twin 1. This twin was first hospitalized at the age of 22 after several months of severe auditory and visual hallucinations and delusions. She was withdrawn, would make bizarre

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comments such as "I'm an airplane," and would talk to people who were not present. While in church she would suddenly start laughing, stating that people were telling her jokes. She would often stare into space while mumbling to herself, and her thoughts were fragmented or loosely associated.

Over the next 3 years she was hospitalized several times and treated with high-potency neuroleptics with minimal or no effect. After nearly 4 years of severe psychosis, haloperidol treatment eventually resulted in improvement. She first came under our care when she was 27 years old, and the haloperidol treatment was discontinued during the course of a research study. She became very psychotic and experienced auditory and visual hallucinations, talking to herself and claiming to be in heaven with angels surrounding her and talking to her. When she was again treated with haloperidol, 20 mg/day, her symptoms almost completely resolved and she was able to work as a secretary for several years. The haloperidol dose was gradually reduced, but at 5 mg/day she suffered a severe psychotic decompensation and was rehospitalized. She was restabilized with haloperidol decanoate injections, 100 mg every 2 weeks. Although not yet able to return to work, she is able to function independently at this time. This patient has been given diagnoses only of chronic paranoid or chronic undifferentiated schizophrenia on the basis of both the Schedule for Affective Disorders and Schizophrenia (SADS) and DSM-III.

Twin 2. This twin was prone to rapid mood swings and angry outbursts since childhood, and at age 19 she developed severe depression and anxiety. She also described a vague sensation that people were staring at her and manipulating her and stated that her vision would become very acute and vivid, although for only very short periods. She once said she felt as though "a force like a boyfriend of mine grabbed me and took me into the bedroom, although no one else was around." She also felt at one point as though her father's emotions would "come through" her but was vague about exactly what this meant. She consistently denied hallucinations, and there was no loosening of associations.

Later in the course of her illness, she described episodes in which she had to go "faster and faster." At one point she wished to give up everything and become an artist, stating that she could be "the greatest artist in the world." She was grandiose, irritable, very talkative, and easily distracted, and she slept poorly. During the course of her illness she was treated with lithium, perphenazine-amitriptyline, haloperidol, thioridazine, desipramine, amitriptyline, fluphenazine, and carbamazepine. None of these medications was clearly effective.

At age 27 she was admitted to a private hospital because she was having severe mood changes, including depression and anger, and suicidal thoughts. Her self-esteem was poor and she felt inferior to others. Her speech was pressured and she fidgeted continually. She was treated with trifluoperazine, although there was no evidence of psychosis. Her mood partially stabilized, and she was discharged on a regimen of trifluoperazine with the diagnosis of schizoaffective disorder.

Later that year she began feeling very depressed and stayed in bed for 4 months. She slept 14 to 18 hours a night, gained 13 lb, and experienced fatigue and loss of energy. She lost interest in many of her hobbies, withdrew socially, and developed feelings of worthlessness and occasional thoughts of suicide. She was noted to spend a lot of time in front of the mirror, and she commented negatively on her appearance, stating she had developed a "cow neck" and severe acne—neither of which was true. Her memory and concentration were poor. She claimed her family was unfair to her, but she could give

no specific examples. She denied having hallucinations or delusions. A SADS interview provided a diagnosis of manic-depressive illness.

Over the following year she had numerous irritable outbursts, depressive episodes, and suicidal thoughts. She never had frank delusions or hallucinations and never manifested the bizarre behavior or fragmentation of thought seen in her twin sister. Occasionally she would have racing thoughts and would strike people without provocation. She was treated with lithium for several months without effect. Over the past several years her mood has stabilized and she has been functioning productively in a secretarial position. Her only medications have been small doses of haloperidol (usually 1 mg/day) for agitation or fluoxetine for depression.

LABORATORY AND INVESTIGATIVE PROCEDURES

Zygoty was determined by blood group analysis at the Immunogenetics Laboratory of Johns Hopkins Hospital, by using the method of Wilson (8). Blood typing is the most reliable method for assigning zygoty to twins (9). The probability of monozygoty was determined to be 0.9999941 (the probability of dizygoty was 0.0000591).

Handedness was determined by using the Edinburgh Inventory (10) and the Annett Handedness Preference Questionnaire (11). Additional tests were used to determine footedness and eyedness. Twin 1 was determined to be fully right-handed, right-footed, and right-eyed, and twin 2 was determined to be fully left-handed, left-footed, and left-eyed.

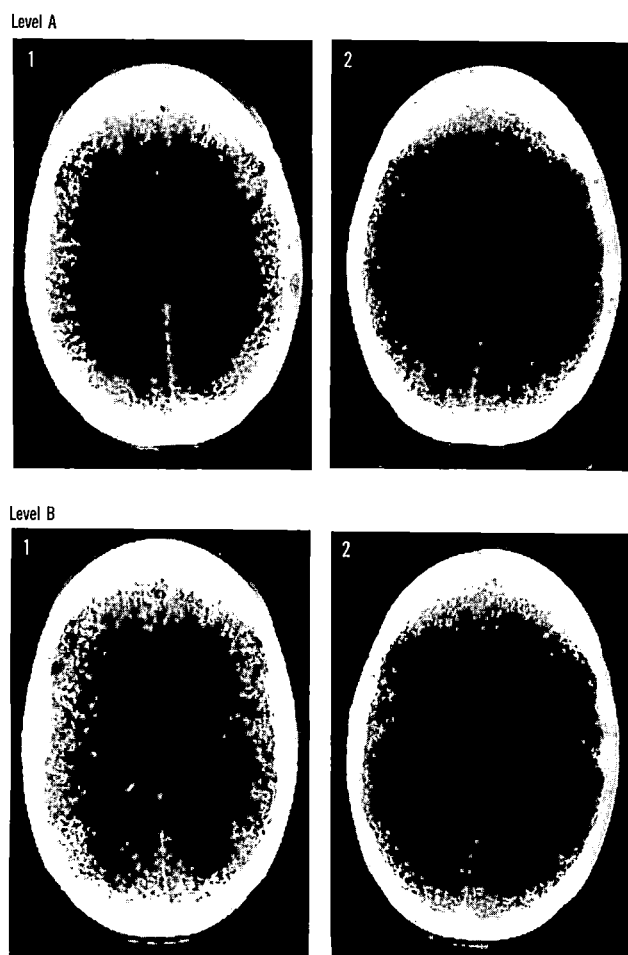
Both twins had 12 years of education. According to the Wechsler Adult Intelligence Scale, their full-scale IQs were 85 and 86, respectively. Twin 1 had a verbal IQ of 89 and a performance IQ of 84, and twin 2 had a verbal IQ of 86 and a performance IQ of 92.

Two slices from the CT scans of the twins, taken at similar levels, are presented in figure 1. The ventricle-brain ratios (VBRs) of twin 1 and twin 2 were 11.6 and 7.9 for the slices at level A and 11.0 and 10.9 for the slices at level B. The occipital regions of the twins appear to be mirror image; twin 1 demonstrates a wider right occipital lobe, and twin 2 has a wider left occipital lobe. When the method of Luchins et al. (12) was applied, the ratios of the left occipital width to the right occipital width for twin 1 were 1.05 (slice A) and 1.11 (slice B), whereas for twin 2 they were 0.94 (slice A) and 0.90 (slice B).

Photographs of the faces of the twins were made and measured according to the method of Sackeim et al. (13). Although several asymmetries were seen, the most interesting asymmetries occurred when the patients smiled. In the measurement of the lateral point of the nostril to the corner of the mouth, twin 1 showed a more pronounced and elevated smile on the right side, whereas twin 2 had a more pronounced smile on the left side.

We performed a standard ridge count and fingerprint pattern examination of the two twins (14). With standard ink techniques hand prints were obtained on both

FIGURE 1. CT Scans of Monozygotic Mirror-Image Twins With Discordant Psychiatric Disorders^a



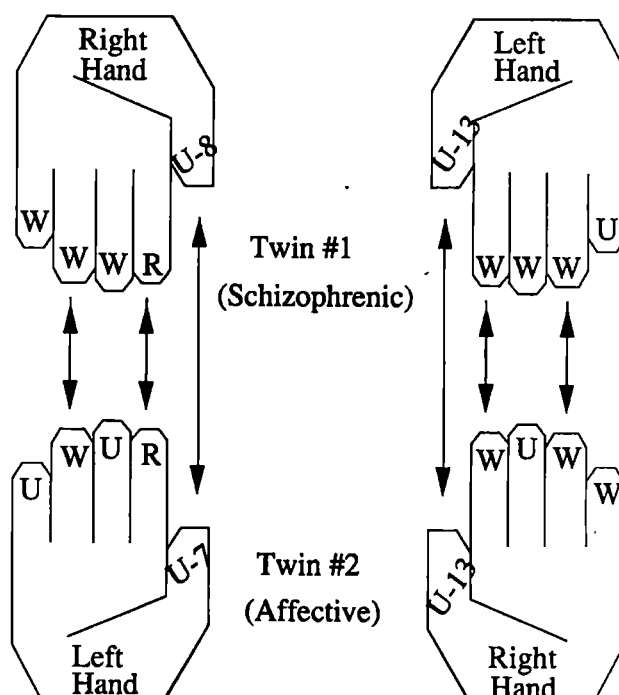
^aTwin 1 (left) had schizophrenia, and twin 2 (right) received diagnoses of bipolar or schizoaffective disorder. The respective scans for the two twins were taken at approximately similar levels. Right and left orientation is the same for all slices, and the right hemisphere is on the reader's left.

hands for both twins. The quality of the fingerprints allowed pattern identification but only incomplete identification of ridge counts. The results available are presented in figure 2. Two facts are evident from examination of the twins' dermatoglyphics: 1) the similarity is greater in the mirror (heterolateral) comparison than in the standard (homolateral) comparison, and this similarity suggests again that these are mirror-image twins; 2) the degree of similarity is low, and the fingerprints do not appear "twin-like," especially in the standard comparison. These monozygotic twins likely would have been misclassified as fraternal in older studies, e.g., the study by Slater (15).

DISCUSSION

Over the 6 years that we have followed these twins, the diagnosis of twin 1 has never been in doubt. Twin 2

FIGURE 2. Dermatoglyphics of Monozygotic Mirror-Image Twins With Discordant Psychiatric Disorders^a



^aThe standard (homolateral) similarity score was 4, whereas the mirror (heterolateral) similarity score was 6 (i.e., higher). U=ulnar loop, W=whorl, R=radial loop.

has had a more confusing clinical picture, initially having symptoms suggestive of schizophrenia but later having symptoms of depression and mania and receiving diagnoses of bipolar or schizoaffective disorder. Although we are not yet prepared to give a definite diagnosis of bipolar illness to twin 2, it is clear that she has had much greater mood instability and much less psychosis than her sister.

Before we discuss the differences in clinical symptoms in these twins, the dermatoglyphic findings deserve comment. Dermatoglyphics have been used in twin studies to help determine zygosity (most such studies were before 1970). The assumption in many of these studies (15, 16) that dermatoglyphics are purely "genetic" markers has since proved to be false. Research since 1970 has shown that dermatoglyphics may be affected substantially by second-trimester prenatal insults, such as rubella, cytomegalovirus, and other viral infections (17). These considerations may have special relevance for monozygotic twin studies of schizophrenia (17, 18). The low dermatoglyphic similarity in this pair of monozygotic twins, whose zygosity was verified by human lymphocyte antigen testing, is consistent with a prenatal insult.

It is not clear why these monozygotic twins have such different presentations. Because twin 1 clearly has schizophrenia, we considered whether twin 2 has an atypical presentation of the same process—perhaps related to a milder prenatal insult, as just discussed. If this

is the case, then two of the possibilities that might account for the different symptoms are that 1) the twins have suffered the same disease process but with different degrees of severity, and 2) the mirroring is in some way related to the symptoms.

Differences in Severity

It is possible that twin 2 simply has a milder case of the same condition afflicting twin 1. This may be reflected in the ventricular size, because twin 1 has larger ventricles than twin 2, which is in keeping with reports of larger ventricles in the schizophrenic members of twin sets discordant for schizophrenia (19, 20) (although patients with mood disorders have also been reported to have large ventricles; see reference 21). Nevertheless, the notion that severity alone can account for the clinical differences strikes us as unlikely. We have observed both twins at different levels of severity throughout their respective illnesses, and they are consistently very different psychiatrically. Twin 1 manifests much more psychosis, and twin 2 demonstrates greater mood lability at all levels of severity.

Differences Related to Mirroring

It is tempting to speculate that the clinical differences may relate to the twins' being mirror images. Whether monozygotic twins become identical or mirror image is believed to be associated with the timing of the egg's splitting. If the egg splits earlier (the rule), both twins will be either right- or left-handed. If it splits later (which is uncommon), they will be opposite handed (22).

We have documented that these twins have opposite handedness, footedness, eyedness, facial asymmetry, fingerprint patterns, and emotional gesturing (asymmetric facial expression when smiling). The twins also have opposite occipital lobe asymmetry. The more commonly observed occipital asymmetry (in which the left occipital lobe is larger than the right) was reversed in the schizophrenic twin but was preserved in the affectively ill twin, a finding that supports previous reports in the literature (12, 23, 24).

If the differences in clinical presentation are in some way related to mirroring, what could be the nature of this relationship? It is possible that the same process affected both twins but the differences in brain organization, related to the mirroring process itself, contributed to the differences in clinical symptoms. For example, one of us (25) has proposed that the left hemisphere may be more susceptible to damage because it lags behind the right hemisphere during certain phases of prenatal development, thus placing it at greater risk for prenatal damage. It is possible that, because of mirroring, in twin 2 it was the right hemisphere that lagged behind and thus suffered more damage. Another possibility is that an asymmetrical insult affected the left hemispheres of both twins. In twin 1, who is right-handed, the damage occurred in a "typi-

cal" left hemisphere, but in twin 2, because of the mirroring, the left hemisphere might actually function more like a right hemisphere. Either of these two possibilities would imply that similar damage might cause either more psychosis or more mood disorder, depending on whether the left hemisphere or the right hemisphere is more affected.

Of course, these are only a few of many speculations that could be made regarding these cases. We believed the cases would be of interest to investigators and clinicians concerned with schizophrenia and mood disorders and to those interested in the importance of neurodevelopment and laterality of brain function.

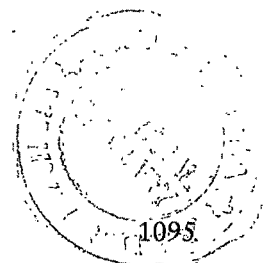
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New Policy Regarding Letters to the Editor

Effective immediately, Letters to the Editor critical of an article published in the *Journal* must be received within 6 weeks of the article's publication; Letters from outside the United States must be received within 12 weeks. Letters received after the deadline will not be considered and will be returned unreviewed.



Interictal Psychiatric Morbidity and Focus of Epilepsy in Treatment-Refractory Patients Admitted to an Epilepsy Unit

Rahul Manchanda, M.B.B.S., M.D., M.R.C.Psych., F.R.C.P.(C), Betsy Schaefer, B.A., Richard S. McLachlan, M.D., F.R.C.P.(C), and Warren T. Blume, M.D., F.R.C.P.(C)

Of 71 consecutive patients admitted to an epilepsy unit of a general hospital, 32 (45%) were classified as having psychiatric disorders by using the General Health Questionnaire. No differences were evident to support a specific relationship between the type or focus of epilepsy and psychopathology.

(Am J Psychiatry 1992; 149:1096-1098)

Several studies attest to higher rates of psychiatric morbidity in epileptic patients (1-4). Furthermore, a particularly strong association between temporal lobe epilepsy and psychiatric disorders has been supported by some investigators (1-3, 5, 6) but not by others (7-10). A general practice survey (4) showed a difference in the frequency of psychiatric disturbance between focal and primary generalized epilepsy but not between temporal and focal nontemporal lobe epilepsy. Thus, the controversy regarding psychiatric illness in patients with temporal lobe epilepsy continues.

This study was carried out primarily to determine whether the prevalence and degree of psychopathology in patients with intractable epilepsy warranted routine psychiatric assessment as part of the investigation for epilepsy surgery. Another aim was to determine whether patients with a temporal lobe focus of seizures have a higher prevalence of psychopathology. Furthermore, the possibility of a relationship between laterality of seizure focus and psychiatric disturbance was investigated.

METHOD

The sample for this study consisted of all consecutive adult (age 16 and older) patients with epilepsy admitted to an epilepsy unit of a general hospital during a 20-month period. All patients were refractory to medical treatment and were admitted for assessment for neurosurgical intervention. Patients were considered treatment refractory if they continued to experience

seizures with an average frequency of at least once every month even with polytherapy using up to three different anticonvulsants for a period of at least 2 years. The seizure disorder was categorized according to the classification of the International League Against Epilepsy (11). All patients had standard EEG telemetry using scalp electrodes with continuous monitoring until sufficient seizures were recorded to delineate the focus. When scalp recordings failed to do this, telemetry was continued with implanted subdural electrodes.

In addition to this standard investigation, all patients were asked to fill in the self-administered 60-item General Health Questionnaire (12). A score of 12 or higher on this questionnaire identifies respondents with a non-psychotic psychiatric illness. The reliability and validity of the questionnaire has been extensively studied (12, 13), and the questionnaire is widely accepted as a screening instrument for defining psychiatric illness in medically ill populations.

RESULTS

Seventy-one patients admitted to the epilepsy unit were included in the sample. Thirty-six (51%) of the patients were men, and 35 (49%) were women. Their mean age was 29 years (SD=10.14). Forty-four (62%) were single, and 23 (32%) were married; four patients were separated or widowed. Their mean age at onset of epilepsy was 12.2 years (SD=9.4), the mean duration of their epilepsy was 16.8 years (SD=8.62), and their mean number of seizures per week was 9.6 (SD=17.8). Thirty-five (49%) of the patients had simple or complex partial seizures, 28 (39%) had simple or complex partial seizures with secondary generalization, and eight (11%) had primary generalized seizures. The primary seizure focus was categorized as temporal in 47 (66%)

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of the patients, nontemporal in 17 (24%), and indeterminate in seven (10%). Differences among these groups on demographic variables were examined by using a chi-square test for categorical variables; no significant differences were found. Of the 47 patients who had temporal lobe epilepsy, 19 (40%) had a left-sided focus, 20 (43%) had a right-sided focus, and eight (17%) were bitemporal.

According to their responses on the 60-item General Health Questionnaire, 32 (45%) of the 71 patients were categorized as having psychiatric disorders (their scores were 12 or higher). When having a General Health Questionnaire score of 12 or higher was compared with the seizure focus by using a chi-square test for comparison of means (table 1), no significant differences were observed ($\chi^2=0.75$, $df=2$, $p=0.69$). When General Health Questionnaire scores and laterality of seizure focus were compared, no significant differences were observed; 10 (48%) of the 21 patients with a temporal focus who were identified as having psychiatric disorders had a left temporal focus, and five (56%) of the nine patients with a nontemporal focus who were identified as having psychiatric disorders had a right nontemporal focus.

DISCUSSION

The highest frequency of psychiatric morbidity in epileptic patients is seen among institutionalized patients and those attending clinics specializing in the treatment of intractable seizure disorders (14). Using the General Health Questionnaire, we identified 32 (45%) of our 71 patients as having psychiatric disorders. These findings are consistent with those of Edeh and Toone (4), whose case material was unselected and community based. However, our results are probably an underestimate given that the sample consisted of a group of patients with more severe, treatment-refractory epilepsy. One or more of the following factors may account for this. Uncooperative, disturbed patients and those with serious psychiatric problems were less likely to be admitted to this inpatient epilepsy unit, where testing procedures require considerable cooperation and patience from the subjects. Furthermore, the General Health Questionnaire is a measure of nonpsychotic emotional illness and does not detect personality disorders.

Gibbs's findings that psychiatric disorders are three times more common among patients with temporal focal epilepsy than among patients with extratemporal focal epilepsy (5) remains controversial (4). This study also fails to support such a claim. In addition, we found no differences based on laterality of the seizure focus, which have been reported by some investigators (15, 16). However, studies supporting relationships between laterality of seizure focus and psychopathology looked at specific aspects of psychopathology that were not assessed in this study.

It may be argued that the General Health Questionnaire measured anxiety related to admission for possi-

TABLE 1. General Health Questionnaire Scores and Seizure Focus of 70 Patients With Epilepsy^a

General Health Questionnaire Score	Temporal Focus (N=47)		Nontemporal Focus (N=17)		Indeterminate Focus (N=7)	
	N	%	N	%	N	%
11 and lower	26	55.3	8	47.1	4	66.7
12 and higher	21	44.7	9	52.9	2	33.3

^aData were missing for one patient with indeterminate focus.

ble neurosurgical treatment. The data do not support this. First, examination of the mean scores on subscales of the General Health Questionnaire shows that although the mean anxiety score was the highest in the total sample, the patients with a General Health Questionnaire score of 12 or higher scored highest on the somatic subscale. Second, our preliminary analysis of the General Health Questionnaire scores of a similar group of patients assessed during hospitalization and 1 year later as outpatients (these patients did not have neurosurgery) did not reveal a significant reduction in General Health Questionnaire scores. Third, even when the cutoff score was increased to 16, no significant findings emerged between localization of seizure focus and having a psychiatric disorder according to the General Health Questionnaire.

There are limitations to the conclusions that can be drawn from this study, however. The sample studied was selected and not representative of a general epilepsy population. The patients were treatment refractory and were admitted to a specialized unit for possible neurosurgical intervention. However, this study has the advantage of a large number of consecutive patients with a well-defined seizure focus. In the past, an apparent excess of temporal lobe epilepsy has been reported in psychiatrically abnormal patients with epilepsy. This study provides an opportunity to examine psychiatric morbidity in a large number of patients with focal epilepsy, both temporal and nontemporal.

Another limitation of this study is that the patients were not clinically evaluated but were assessed by using the General Health Questionnaire. This is because the study was essentially a pilot project to determine whether detailed psychiatric assessments are warranted in every candidate for epilepsy surgery (17). The General Health Questionnaire is essentially a screening test, but it does represent a general measure of nonpsychotic psychopathology in a medically ill population. Therefore, a conclusion that 45% of patients have psychiatric morbidity would at best be an approximation. However, it is also an indication for us to carry out detailed preoperative assessments on this group of patients.

All patients currently admitted to the epilepsy unit undergo a psychiatric diagnostic interview and standardized rating scale assessments to determine whether such data can predict postoperative emotional status and adjustments. The data from these evaluations will be forthcoming in the near future.

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Neurobehavioral Functioning in a Nonconfounded Group of Asymptomatic HIV-Seropositive Homosexual Men

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Neurobehavioral functioning was tested in 34 asymptomatic HIV-seropositive and 43 HIV-seronegative male homosexual subjects without substance abuse and CNS disorders. The HIV-positive subjects exhibited mild motor slowing compared to the seronegative subjects. These differences remained after controlling for potential cofactors. Early neurobehavioral impairment in HIV infection seems limited to subclinical motor deficits and attributable to HIV rather than possible confounding factors.

(Am J Psychiatry 1992; 149:1099-1102)

It is known that many patients with AIDS suffer from neurobehavioral dysfunction, including impairment of memory, language, information processing, attention, and motor function. While several reports have suggested that subclinical impairments may exist early in the course of HIV infection before other clinical signs and symptoms of AIDS appear (1-4), other investigators have not replicated these findings (5-7). Recent studies have suggested that if asymptomatic HIV-seropositive individuals exhibit neurobehavioral deficits, coexisting factors such as depression (8) or vitamin B₁₂ deficiency (9) may be the cause. Wilkins et al. (10) suggested that neurobehavioral impairment in asymptomatic HIV-positive persons may be due to confounding variables such as limited education or previous histories of substance abuse, learning disability, traumatic brain injury, or other CNS disorders. Furthermore, it has been suggested that immunosuppression precedes any neurobehavioral impairment (11).

The goals of this study were 1) to assess the impact of several potential coexisting factors on the early presentation of neurobehavioral impairments in HIV infec-

tion and 2) to examine these relationships in a group of subjects without confounding variables.

METHOD

The study was conducted as part of a larger investigation, the Coping in Health and Illness Project. The participants were 34 asymptomatic HIV-seropositive homosexual men and 43 HIV-seronegative homosexual male comparison subjects. Subjects were included if they were between the ages of 18 and 50 years, spoke English as their primary language, and had completed at least 10 years of schooling. HIV-positive subjects were included if homosexual contact was their sole risk factor for infection and if there were no clinical symptoms of immunosuppression. Strict exclusion criteria were used to preclude the confounding effects of substance abuse, mild head injury, learning disability, attention deficit disorder, or any preexisting CNS disorder (with the exception of occasional migraine headaches). Potential subjects were also excluded if they had ever taken zidovudine or if they had taken any medication other than acetaminophen during the 2 weeks before the study began. In addition, potential subjects were excluded if they had any significant past or present medical illness (e.g., heart disease, diabetes, endocrinopathies, autoimmune disorders, lung disease) or if they had undergone major surgery in the previous 6 months.

All potential subjects were administered a modified version of the Structured Clinical Interview for DSM-III-R (SCID) (12). Individuals with past or present psychotic disorders were excluded. Only five subjects not excluded on the basis of past or current nonpsychotic

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TABLE 1. Neurobehavioral Function Scores^a of Asymptomatic HIV-Seropositive and HIV-Seronegative Male Homosexual Subjects

Function	HIV-Positive Subjects (N=34)		HIV-Negative Subjects (N=43)		p ^b		
	Mean	SD	Mean	SD	ANOVA ^c	ANCOVA ^d	ANCOVA ^e
Attention and information processing	3.0	1.3	2.5	1.0	<0.05	n.s.	n.s.
Executive function	2.6	1.3	2.2	0.9	n.s.	n.s.	n.s.
Motor function	2.9	1.3	2.2	0.6	<0.01	<0.05	<0.05
Language	2.1	0.8	1.8	0.6	n.s.	n.s.	n.s.
Visuospatial function	2.8	1.5	2.6	1.2	n.s.	n.s.	n.s.
Learning and memory	3.1	1.4	2.7	1.1	n.s.	n.s.	n.s.
Global impairment	3.5	1.3	2.8	1.0	<0.01	n.s.	n.s.

^a1=no impairment; 9=severe impairment.^bAll tests were one-tailed.^cAnalysis of variance, no covariate.^dAnalysis of covariance with education covaried.^eAnalysis of covariance with education, socioeconomic status, Hamilton Rating Scale for Depression score, vitamin B₁₂ level, and CD4 cell count covaried.

axis I disorders fulfilled criteria for any psychiatric illness. These included one subject (2%) who was HIV negative and four (12%) who were HIV positive, all with major depression. (Specific exclusion criteria are available from the first author on request.)

The groups were similar in age (HIV positive, mean=30.1 years, SD=7.1; HIV negative, mean=32.2 years, SD=7.0), although the seronegative group had completed more years of schooling (HIV positive, mean=14.3, SD=2.5; HIV negative, mean=16.4, SD=2.2). All participants provided informed consent.

The subjects underwent a comprehensive neuropsychological evaluation. Following the guidelines of the National Institute of Mental Health Workshop on Neuropsychological Assessment Approaches (13), two experienced neuropsychologists (R.A.S. and H.J.R.) who were blind to the subjects' HIV status provided summary ratings for the following neurobehavioral domains: 1) attention and information processing, 2) executive function, 3) motor function, 4) language, 5) visuospatial function, and 6) learning and memory. In addition, a global impairment rating was given. Ratings were based on examination of raw test data, comparison of these data with published and internal norms, and written descriptions of behavioral observations. The two sets of ratings were averaged to create seven "function scores," each ranging from 1 (no impairment) to 9 (severe impairment).

Between-group differences were assessed first by analyses of variance and then by analyses of covariance. Covariates were education (years of schooling), socioeconomic status (Duncan's Revised Socioeconomic Index score [14]), depressive symptoms (score on the 17-item Hamilton Rating Scale for Depression), vitamin B₁₂ deficiency (plasma B₁₂ level), and immune status (CD4 cell count).

RESULTS

Without any covariates, the HIV-positive subjects performed significantly worse than HIV-negative sub-

jects on a variety of neuropsychological functions. With education covaried, significant group differences were found only on summary ratings of motor function and on individual motor function tests. This was expected because of the between-group differences in education level and the high correlations typically found between level of education and verbal skills (e.g., abstraction, naming, vocabulary, verbal memory).

The significant differences in motor function remained when each of the other covariates was controlled individually and when all covariates were included in the analyses simultaneously (tables 1 and 2). The differences observed on the 2 & 7 Test (a timed measure typically viewed as assessing selective attention) were due to the HIV-positive subjects' lower performance speed across conditions rather than attentional dysfunction (e.g., errors of omission).

DISCUSSION

In this group of asymptomatic HIV-positive homosexual men without the confounding factors of substance abuse, head injury, learning disability, zidovudine use, or preexisting CNS disorder, motor slowing was the only observed neurobehavioral deficit. It should be stressed that the motor dysfunction exhibited by these subjects was very mild and most likely would not affect their ability to carry out daily activities. There was no evidence of slowed information processing, memory impairment, or attentional dysfunction, as has been suggested by previous studies with more heterogeneous samples. The observed motor differences could not be accounted for by previously implicated factors such as education, socioeconomic status, depression, vitamin B₁₂ deficiency, or immune status. It is important to note that there were no significant group differences in Hamilton Depression Rating Scale scores, and neither group's mean score fell in the depressed range. Similarly, vitamin B₁₂ deficiency was infrequent (less than 10% of either group had levels less than 200 pg/ml). This may be due to the fact that our HIV-posi-

TABLE 2. Scores on Individual Tests of Neurobehavioral Function of Asymptomatic HIV-Seropositive and HIV-Seronegative Male Homosexual Subjects

Function/Test	HIV-Positive Subjects (N=34)		HIV-Negative Subjects (N=43)		p ^a		
	Mean	SD	Mean	SD	ANOVA ^b	ANCOVA ^c	ANCOVA ^d
Attention and information processing							
Corsi Spatial Span							
Forward	5.9	1.0	6.1	1.1	n.s.	n.s.	n.s.
Backward	5.4	1.3	5.7	1.1	n.s.	n.s.	n.s.
2 & 7 Test							
Controlled search	129.6	19.6	139.3	18.9	<0.01	<0.05	<0.01
Automatic detection	142.4	23.1	160.0	23.7	<0.001	<0.01	<0.05
Paced Auditory Serial Addition Test							
Series A	40.4	8.7	41.3	7.7	n.s.	n.s.	n.s.
Series D	26.0	8.7	28.1	7.2	n.s.	n.s.	n.s.
Digit Symbol, age corrected	11.5	2.3	12.3	2.0	<0.05	n.s.	n.s.
Executive function							
Trail Making							
A, time (seconds)	24.9	8.1	22.1	6.3	<0.05	n.s.	n.s.
B, time (seconds)	57.5	23.4	56.2	30.1	n.s.	n.s.	n.s.
Verbal Fluency, adjusted score	47.6	13.9	49.3	12.2	n.s.	n.s.	n.s.
Stroop Color-Word Test, interference time (seconds)	105.6	25.8	104.8	18.7	n.s.	n.s.	n.s.
Shipley Abstraction, T score	55.6	8.4	59.7	6.2	<0.01	n.s.	n.s.
Motor function							
Finger Tapping							
Dominant hand	51.5	7.1	54.6	4.6	<0.05	n.s.	<0.05
Nondominant hand	46.5	5.6	49.6	4.8	<0.01	<0.05	<0.05
Grooved Pegboard							
Dominant hand	62.7	8.9	59.0	5.8	<0.05	n.s.	<0.05
Nondominant hand	74.7	13.9	69.2	7.6	<0.05	n.s.	n.s.
Language							
Shipley Vocabulary, T score	52.7	7.6	56.0	6.3	<0.05	n.s.	n.s.
Boston Naming Test, total score	27.7	2.1	28.5	1.4	<0.05	n.s.	n.s.
Visuospatial function							
Block Design, age corrected	11.1	3.2	12.1	2.5	n.s.	n.s.	n.s.
Complex Figure, copy	29.3	3.8	29.8	3.2	n.s.	n.s.	n.s.
Learning and memory							
Complex Figure							
Immediate recall	21.5	7.7	21.5	5.6	n.s.	n.s.	n.s.
Delayed recall	20.8	7.4	20.6	5.6	n.s.	n.s.	n.s.
California Verbal Learning Test							
Total correct, trials 1-5	56.8	9.8	60.3	8.0	<0.05	n.s.	n.s.
Long delayed free recall	13.0	2.0	13.0	1.9	n.s.	n.s.	n.s.

^aAll tests were one-tailed.^bAnalysis of variance, no covariate.^cAnalysis of covariance with education covaried.^dAnalysis of covariance with education, socioeconomic status, Hamilton Rating Scale for Depression score, vitamin B₁₂ level, and CD4 cell count covaried.

tive subjects were studied early in the course of HIV infection and met strict inclusion criteria. In a more heterogeneous group, these factors might have more influence on neuropsychological performance. These findings are based on a relatively small study group and therefore may not be generalizable to the larger population of HIV-infected individuals. Replication of these results in larger groups of subjects similarly lacking potentially confounding factors is necessary.

In summary, mild motor slowing may indicate CNS disturbance early in the course of HIV infection. This finding is consistent with recent reports of early CNS involvement in HIV. For example, cellular immunity has been found to diminish in the CNS before it does so in blood (15), and abnormalities in cerebrospinal fluid (16) and evoked potentials (17) have also been reported

in asymptomatic HIV-positive individuals. However, due to recent reports of peripheral nervous system involvement early in the course of HIV infection (18), further investigation of the underlying causes of HIV-related motor dysfunction is needed.

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Book Forum

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ETHICS AND LAW

Psychoanalysis and Ethics, by Ernest E. Wallwork. New Haven, Conn., Yale University Press, 1991, 344 pp., \$35.00.

Ernest Wallwork, a professor of ethics and a candidate in a psychoanalytic training institute, undertakes what might be considered a quixotic effort to at least modify the prevailing perception that psychoanalysis, with its bleak portrayal of the egoistic, narcissistic, and aggressive roots of human behavior, is an amoral discipline that allows no basis for either a philosophical or a practical theory of morality. In his preface, Wallwork promises an "accurate and sympathetic" reading of Freud that will justify a radical new interpretation of Freud and morality.

Wallwork is aware that his first task is to take a fresh look at the Freudian concepts of determinism, egoism, and narcissism, which stand as the primary roadblocks to his reevaluation. He begins by discussing the confusion in understanding Freud's writings engendered by the failure to take into account the differences between the metapsychological and clinical theories of psychoanalysis. Furthermore, neither professional philosophers nor psychoanalysts, for differing reasons, have expended much effort in trying to discern a philosophical basis for morality in Freud's writings. What of the apparent paradox derived from the conflict between Freud's alleged "hard" determinism and his assertion that the goal of psychoanalysis is to augment the freedom of the patient to make choices? Wallwork attempts to resolve this paradox by demonstrating that the psychic determinism of psychoanalysis, whose goal is to interpret clinical data, is not the same as the physical determinism of the sciences, which attempt causal explanations. Furthermore, unconscious motivations, although certainly very potent influences, especially when unacknowledged, are not the only determinants of human behavior, especially when the maturing ego gains some autonomy from their demands and sponsors a consequent growth of individual responsibility.

Wallwork then turns to psychological egoism, another of the preserved keystones of psychoanalytic amorality because, to the extent that individuals are under the domination of the pleasure principle, they attend only to their own self-interest and are incapable of any genuine concern for others. But the pleasure principle, leading to an unaltered psychological hedonism, is not the only factor influencing human behavior. It must give way partially to the reality principle, which at least allows the replacement of short-range by long-range satisfactions. Mature human goals extend toward happiness, of which pleasure is only a component, and this goal allows the interests of others to take their place along with self-satisfaction.

Wallwork answers the contention that we are so moved by narcissistic self-love that moral motivation is impossible by pointing out that narcissism is not limited to self-absorption and egoism but can also broaden to include self-love and self-regard. With maturation, and especially after the introduction

of eros in the second instinct theory, barriers to the existence of nonegoistic motives and love for others can at least be weakened. But we must still ask whether object love can be nonegoistic and other-regarding or whether this is impossible in the context of drive theory with self-satisfaction, immediate or delayed, as the only goal. As he does throughout the book, Wallwork answers this question by showing the progression in Freud's ideas and theories throughout his long career, especially after 1920 and "Beyond the Pleasure Principle" (1). Drives seeking only self-satisfaction can be transformed through aim inhibition and sublimation to form genuine other-regarding sentiments, providing room for the nonsensual elements of love alongside the sensual component. These allow the development not only of romantic love but also of group solidarity and social interests. Thus, it can be said that the relative benevolence of eros, while not eliminating egoistic instinctual demands, tempers and broadens love to include affectional elements in intimate relationships and benevolence and altruism in social relationships.

Is psychoanalysis of any value as a normative discipline with regard to ethical and moral standards? Freud disagreed violently with the "love commandment" that you should love your neighbor as yourself, asserting that it is impossible, unjust, indiscriminate, actually promotes hostility, and causes unhappiness. His arguments for these condign judgments are cogent, but Wallwork attempts to show that they are directed against a narrow interpretation of the love commandment (one may wonder whether Freud's hostility toward religion also played a role). Wallwork claims that Freudian doctrine may be quite compatible with a broader version of the love commandment that emphasizes nonmaleficence over a hypocritical universal love. Freud certainly would have preferred the doctrine of Hillel, not to do unto others what one would not like to have done to oneself, over the Golden Rule.

Can the allegedly value-free stance of psychoanalysis be compatible with an effort to use it for elucidating moral standards? Analysts take an avoidance of moral judgments as an article of faith and the only acceptable treatment posture. However, at least implicitly, psychoanalysis shares the values of science and of the healer, and analytic neutrality is not an end in itself but a device to encourage the patient's autonomy and freedom to choose. Also implicit in psychoanalytic technique are the moral rules of full disclosure, keeping promises, absence of sexual or other exploitation of the transference, and confidentiality. But even if psychoanalysis cannot avoid dealing with value judgments in its therapeutic endeavors, it still may be claimed that the discipline has nothing to contribute to the justification of these values. This is because of the relativistic implications of the superego, which asserts moral claims only on a basis of rewards and punishments, and the weakness of the ego, which is capable only of exerting an indirect bureaucratic power in finding somewhat more socially acceptable outlets for id desires. Wallwork responds to these contentions by denying that the ego is so weak or incapable of using rational grounds as a basis for moral decisions.

Freud was in vigorous favor of a rational and secular basis

for ethics and would not countenance any ontological grounds, either religious or philosophical, because moral principles must be generated from the human needs for happiness and love. He disagreed with Kant's assertion that reason and duty should be the only grounds for morality. Reason plays a part but must be balanced by human wishes, needs, and emotions. Although, rather surprisingly, Freud can be seen as holding the optimistic view that most people possess an other-regarding core as a basis for moral behavior, he had no doubts that this must be weighed against equally strong cruel and egoistic tendencies. The two opposing trends must contend with each other because "belief in the goodness of human nature is an evil illusion."

Can psychoanalysis identify the practical, personal reasons that should serve as normative guides to the way an individual should live in trying to achieve happiness, the ultimate good? Freud comes up with 11 paths to this goal. These paths are positive and negative and include both sexual and nonsensual modes. Possibly they can be summarized in Freud's succinct paradigm of "love and work."

Psychoanalysis, at least in Wallwork's reading of Freud, can contribute to the justification of moral principles from the social as well as the personal standpoint. Social rules are certainly necessary to protect against the ravages of naked instinctual urges, but they will be ineffective unless they are buttressed by the libidinal bonds of eros. Although the need to renounce aggressive and sexual satisfaction in the service of group aims inevitably constricts the possibilities for happiness (civilization must have its discontents), Freud offers a consolatory hope that the inevitable individual-versus-group conflicts can progressively be ameliorated by evolutionary developments. Meantime, a reasoned ethic for divided humans comprises the virtues of nonmaleficence, limited benevolence, honesty, promise keeping, autonomy, and justice. The criticism that for Freud justice is just a "mask for envy," a kind of dog in the manger ethic, may be answered by Freud's writings advocating the rule of law, equal treatment, liberty, distributive justice, and just war considerations even though adherence to these abstract principles will always be limited by man's animal heritage. Utopian hopes like communism will inevitably fail because of an erroneous view of human nature.

Much of the above can be summarized by stating that although man's instinctual egoistic core inevitably limits his ability to conform to "higher" and other-regarding principles, man is capable also of transcending the dominance of these elements by modifying their effects through aim inhibition and sublimation and through the influence of eros, which permits the possibility of altruistic behavior even at an instinctual level.

In *Psychoanalysis and Ethics*, Wallwork makes a formidable case for his position that Freud's views on morality and ethics are far more complicated and sophisticated than those attributed to him by his critics, and Wallwork seems to have succeeded in dispelling the notion that psychoanalysis is simply amoral and incapable of being used to explore the roots of ethics and morality. Wallwork accomplishes his purpose through a careful and even encyclopedic exegesis of what Freud said about the various subjects treated in the book. He repeatedly points out that Freud's critics, like Rieff, ignore statements by Freud that counterbalance the statements they quote. The salutary emphasis on how Freud's views changed during the evolving theoretical stages of his career serves as a corrective to simplistic views of Freud's theories.

Wallwork, I believe, has accomplished his purpose of "at least partially persuading" the reader to look at Freud, psy-

choanalysis, and morality in a different way. It seems clear, however, that Wallwork very much wants psychoanalysis to be freed from its burdensome reputation for amorality. Therefore, although he is by no means uncritical, his "sympathetic" attitude may raise questions about his objectivity. He perhaps neglects the point that even the apparent amorality of psychoanalysis has a moral effect when revelation of hidden motives deflate hypocritical moral pretensions. Wallwork appears totally accepting of Freudian clinical theories and findings, and he accepts as gospel such suspect theoretical entities as psychic energy. He also appears a bit naive in his infrequent references to clinical areas.

Psychoanalysis and Ethics is cogently reasoned and densely footnoted, even to the point of impeding the reading of this almost entirely abstract book. It is an impressive piece of work that may change the way Freud's concepts of morality are regarded. It will well repay the interest of those in the professional and intellectual world who take these matters seriously.

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Clinical Handbook of Psychiatry and the Law, 2nd ed., by Paul S. Appelbaum, M.D., and Thomas G. Gutheil, M.D. Baltimore, Williams & Wilkins, 1991, 408 pp., \$55.00.

The first edition of this excellent book was published in 1982. The authors have retained the format, the subjects covered, and much of the text material—wise decisions because they were so well presented and received. The book is geared toward clinical practice. The chapter subjects are confidentiality and privilege, legal issues in emergency psychiatry, legal issues in inpatient psychiatry, malpractice and other forms of liability, competence and substitute decision making, forensic evaluations, clinicians and lawyers, and the clinician in court. Each chapter is divided into seven sections: case examples, legal issues, clinical issues, pitfalls, case example epilogues, action guide, and suggested readings.

Here is a tip in reading this book. Resist the temptation to go directly from the cases to the epilogues. This generates considerable suspense, which makes for exciting reading, and the epilogues are more meaningful after the clinical and legal issues are clearly explicated.

There have been new developments since the 1982 edition. Gutheil and Appelbaum are now Appelbaum and Gutheil. The suggested readings have been substantially revised, enlarged, and brought up-to-date. Discussion of child custody has been eliminated; "readers are referred to one of the excellent texts available that now address the full range of child psychiatry and law issues."

Several new case vignettes have been added. There is one concerning a 28-year-old newly married man who is HIV positive, wants to have a child, but does not want to inform his wife of his HIV status. The ethical issues involved and the clinician's dilemma and its resolution are presented in the epilogue. This is the only reference to AIDS in this book, which is my one disappointment in this fine work. From where I sit, AIDS presents so many ethical and legal problems to psychia-

trists and other clinicians that I would have welcomed a fuller discussion of these overwhelming problems by such lucid and well-informed authors.

Recent court cases are cited. For instance, in discussing competence to consent to voluntary hospitalization, the authors comment that "a recent U.S. Supreme Court decision (*Zimmerman v. Burch*) may draw increased attention to this issue. The Court held that in those states, such as Florida, that require patients to be competent before signing in voluntarily, the failure to screen out incompetent patients violates these patients' constitutional rights. It is unclear whether the court would actually restrict voluntary hospitalization only to those patients found competent, assuming a state's statute is silent on the issue."

Important regulatory and legislative developments are also cited. In the chapter on malpractice and other forms of liability, the authors note,

In response to the perception that the professions have been ineffective in sanctioning sexual activity with patients, the states have become much more aggressive. Complaints to boards of registration routinely result in therapists losing their licenses. A growing number of states are passing laws requiring the reporting of sexual activity that becomes known to other health and mental health professions, and making it easier for patients to sue (e.g., defining the cause of action, extending the statute of limitations) and even criminalizing the behavior. Therapists found to have had sex with patients, and in some cases former patients, now face long prison terms in some states.

Some wording has also been improved since the first edition. In the chapter on the clinician in court, the authors in 1982 wrote about the "direct examination of the patient." In 1991 they substitute "the direct examination of the subject." This is surely more accurate because many individuals receiving forensic examinations are not "patients" in the generally accepted meaning of the term.

I highly recommend this book to all psychiatrists and other mental health practitioners. The many ways in which the law impinges on clinical practice are succinctly and brilliantly described. The methods by which the clinician can most effectively operate in these circumstances are clearly described and should be most helpful to all concerned.

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Alzheimer's Disease Research: Ethical and Legal Issues, edited by Joseph M. Berg, Harry Karlinsky, and Frederick H. Lowy. Toronto, Carswell, 1991, 354 pp., \$45.95 (C).

This work is the product of a symposium held in Toronto in 1989 on legal and ethical issues relating to Alzheimer's disease research. Unlike many symposium proceedings this work has been well edited and provides a balanced overview of legal and ethical issues relating to Alzheimer's disease research. Although the U.S. perspectives on legal issues are covered adequately, this book is clearly a Canadian product. Yet those of us who live south of the border would be wise to read how the Canadians approach these issues from their own perspective.

The work is divided into three main sections. First there is

a section on involving patients in research. Issues covered are primarily those of informed consent and alternatives to patients' giving consent themselves. Next there is a major effort devoted to ethical and legal issues arising from specific areas of Alzheimer's disease research. The general areas covered include etiological (including genetics), pathophysiological, diagnostic, and treatment-related research. The work concludes with a section on overall guidelines based on the current status of the field.

All in all I found this to be a worthy reference work that should be of use to those performing research in Alzheimer's disease, to those in the legal profession who define criteria for informed consent and other related issues, and to those on human subjects committees, who invariably will ask prospective Alzheimer's disease researchers the questions raised in this book.

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Decision Making in Psychiatry and the Law, by Thomas G. Gutheil, Harold J. Bursztajn, Archie Brodsky, and Victoria Alexander. Baltimore, Williams & Wilkins, 1991, 265 pp., \$36.00.

Just how are decisions about psychiatry made in the legal system? Dr. Gutheil and his colleagues at the Program in Psychiatry and the Law of the Massachusetts Mental Health Center and Harvard Medical School examine, by survey and interview, the factors that inform or produce a malpractice case involving suicide, the decision to commit a mentally ill patient involuntarily, the making of treatment decisions, and the determination of competence.

The malpractice case, based on an actual event, is designed as a heuristic exercise to highlight areas of decision making in psychiatry and the law. It is the opening chapter, and it reads like a novel, with dialogue setting out the risk-versus-benefit analysis of the situation. The doctor muses, "Will the patient be so dismayed by the experience of being involuntarily hospitalized that she despairs, resulting in an increased risk of suicide? Will 'taking over' for the patient intensify her feelings of helplessness?" And so forth. Thinking of all these possibilities, although stimulating for a seminar, may prompt the clinician to turn to a fortune cookie.

How do clinicians and judges weigh the risk and benefits of antipsychotic medications? How is the principle of triage (allocation of limited resources) used and misused in making decisions about "difficult" patients? Why do some patients decide to refuse treatment, and what are the clinical implications of validating or challenging treatment refusal? To answer these questions, the authors presented psychiatrists and judges (who were attending seminars on medicolegal issues) with clinical vignettes, asking them to assign weight to the risks and benefits.

As the authors point out, fantasies about treatment and the law and the wish for legally defensible procedures may lead to clinically inferior practices. Defensive medicine brings with it increased costs (but, when covered by insurance, it adds to income).

In commitment decisions, as every practitioner knows, psychiatrists tend to second-guess judges and judges tend to rely on psychiatric opinion. The authors call it "a type of role-switching." The authors' studies confirm that, in approaching commitment decisions, clinicians assume a judicial role by anticipating the judge's ruling on a case and judges assume a

clinical role by relying on the psychiatric evaluation and on extra-statutory factors concerned with compliance.

In dealing with treatment refusal, psychiatrists may feel "caught between torts." On one side are laws that protect patients against being treated against their will, and on the other side are laws that protect patients from negligence caused by lack of treatment.

Are psychiatrists and other physicians being literal-minded about the law? They have "respect for the law," which they tend to interpret to mean a literal reading of the law; hence, they question any tactical maneuvering in a case or any result-oriented decision. Persons labeled "schizophrenic" are known to be concrete in language and thought, but, curiously, psychiatrists on the whole seem to take a similar concrete-minded approach in interpreting rules of law.

Working from an interdisciplinary framework, the authors have produced a sophisticated and well-written book. They illustrate the various factors, subtle or otherwise, that go into the making of a decision. This is not a book for those who want firm and simple answers.

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HISTORY OF PSYCHIATRY

Utopia, Community Care, and the Retreat From the Asylums, by Dylan Tomlinson. Philadelphia, Open University Press (New York, Taylor & Francis, distributor), 1991, 176 pp., \$70.00; \$29.95 (paper).

The reasons for closing state psychiatric hospitals in the United States is no grand mystery. States continue to shut down state beds and close state hospitals as a stratagem for shifting the fiscal burden of care of the patients from state government to the federal government (predominantly Medicaid and Medicare). Dylan Tomlinson's book is about the closing of public psychiatric hospitals in England, where the reasons for doing so are somewhat more complex even if the final product is equally as poorly thought through as the American version.

Tomlinson is a sociologist who worked with the Team for Assessment of Psychiatric Services evaluating what happened to 278 patients discharged between 1985 and 1988 from London's Friern and Claybury public psychiatric hospitals. Both hospitals were scheduled to be closed as part of the English trend in this direction; Barnstead, Powick, and Exeter hospitals had already been closed. For mental health professionals interested in this issue the book is worth obtaining for its details of the planning and politics that accompany such social service experiments. In Tomlinson's words, the hospital closings were predicated on "the revolutionary proposition . . . that all patients could live in community units outside asylums, and that their placements could be funded from the revenue sunk into the big hospitals" (p. 64). Probably never in the history of social services have such massive experiments been carried out with so little data or so little follow-up.

The Team for Assessment of Psychiatric Services was an effort to provide such follow-up, but methodologically it was quite unsatisfactory. The patients initially selected for discharge were those who were "more articulate and interested in moving" (p. 149), the best bets for community placement and thus not representative of all patients scheduled to be discharged. Furthermore, the team placed much emphasis on the

discharged patients' own statements that they did not wish to leave their group homes once placed there. Anyone who has worked with this patient population knows that many of them are very resistant to changes of venue and are likely to want to stay wherever they are at the time.

A true measure of what happens to these patients must take into account the number of their daily social contacts, opportunities for activities, opportunities for rehabilitation and work, and similar measures. There is no question that a large number of patients who have been deinstitutionalized from public psychiatric hospitals are better off than they were in the hospital, but this applies predominantly to the least impaired patients, such as this study encompasses. It is not at all clear that the more severely impaired, who have been merely "trans-institutionalized" to nursing homes or large, dreary group homes, are any better off, to say the least. What is probably most discouraging about this book is that England seems to be intent on replicating the worst, as well as the best, aspects of the American deinstitutionalization experiment.

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Menninger: The Family and the Clinic, by Lawrence J. Friedman. New York, Alfred A. Knopf, 1990, 450 pp., \$29.95.

Lawrence Friedman, Professor of History and American Studies at Bowling Green State University in Ohio and a three-time recipient of fellowships from the National Endowment for the Humanities, has written a "triple-header" biography. First, this book concerns the individual as well as the family history of the Menningers, a distinguished family of psychiatrists now into the fourth generation of specialists in the field. Second, Professor Friedman gives us a slice of the history of American psychiatry during its critical and transitional years. Finally, we read about general American history of this specific time, particularly the changes that occurred in rural mid-America. With clarity and detail, and yet totally involving, the biographer presents us with facts, impressions, positive and negative issues that arose over the years, and in-depth portraits of key Menningers as well as the many nonfamily professionals who interacted with and were trained by the Menningers at the Clinic and the School and then moved to all parts of the United States and other countries.

The Menninger Clinic welcomed refugee colleagues who came here from Europe and helped them reestablish their personal and professional lives. Just as many came to Topeka, now the Clinic is establishing branches in other locations in the United States—migration goes in more than one direction. In many ways we find parallels between the Menninger institutions and programs and those organized and operated by the Mayo Clinic.

Having had the privilege of knowing members of the last three Menninger generations as well as many others who were educated and trained in Topeka, I can attest to the dedication, honesty, excellent clinical care, and path-breaking research that is associated with the Menninger Clinic, School, and Foundation.

Professor Friedman highlights details of the frontier areas discovered by the Menninger immediate and extended family, as well as other pioneers of the time, and includes the support given to other disciplines involved with mental health and illness. Through access to archives, private papers, personal interviews, and government reports, the reader gains an appreciation of "the influence of family dynamics upon institutional

activities" in the years before World War II and how during the subsequent decades the institution expanded and formally became a nonprofit foundation devoted to education, research, publications, and clinical activities. The author's emphasis is on the evolution and connections between the early family members and the organization that has emerged and continues to keep pace with the major advances in the mental health field.

Professor Friedman began the research that resulted in this excellent volume in 1981, when he came to Topeka to participate in the Menninger Interdisciplinary Studies Program. He was formally given permission to "see all" in March 1982. Patient records and diagnostic data were "off bounds," but he was given access to organizational and personal files, including letters and documents. "Karl honored my request to reveal everything that was relevant to my narrative" (p. xiv). "The openness of the Menningers . . . was courageous. They knew that serious scandals and other shortcomings in their history would be presented and that public awareness of these details might affect patient referrals, staff recruitment, and private donations" (p. xiv). This has not occurred. In fact, as testimony to the very professional ethics and ideals that exemplify the Menninger institutions, this book has and will add to their already gigantic stature and reputation.

The "scholar's dream" was not one-sided—methodological dilemmas presented themselves. Professor Friedman, I believe, has successfully dealt with these. He fulfilled his scholar's dream by carefully obtaining an overwhelming amount of information. He traveled to or corresponded with other institutions, talked with dozens of individuals who candidly shared their information and impressions with him, was allowed to read heretofore sealed documents, and received countless telephone messages. We can read in this condensed but flowing narrative a synthesis of newer methodological approaches to historical and biographical research. The processing of the information and then the clear, lucid presentation of what the historian-biographer has learned resembles the approach the psychoanalyst uses with data obtained in the treatment setting. Professor Friedman correctly states, "This was a very difficult book to research and to write" (p. xvii), but he did it in exemplary fashion. It will be a model for future reports of the history of institutions and the biography of individuals worthy of the efforts and work seen in this book.

I have refrained from giving details, simple and complex, about the contents of the book. The time and energy of the interested reader will be amply rewarded. The careful notes (almost 100 pages in length), the bibliographical notes, and the excellent index enhance the value of an already very valuable piece of work.

The Menninger institution continues to grow, expand, and develop. In a recent issue of the *Menninger Perspective*, Glen Gabbard, M.D., Vice-President for Adult Services of the Menninger Clinic and Director of the C.F. Menninger Memorial Hospital, reported that the Menninger organization now has "more than 1,200 employees on two campuses in Topeka and in satellite clinics in San Francisco, Phoenix, Tampa, and Kansas City" (1). In this same issue, the new organizational structure was announced (2). Dr. Roy Menninger, son of Dr. Will, is President and Chief Executive Officer of the parent Menninger Foundation. His brother, Dr. W. Walter Menninger, is the President and Chief of Staff of the Menninger Clinic. Thus, two Menninger brothers again head the institution that was started and developed by two earlier Menninger brothers, Dr. Karl and Dr. Will. In a sense, we are having durable continuities in a major American institution.

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PERSONALITY

Psychobiology of Personality, by Marvin Zuckerman. New York, Cambridge University Press, 1991, 400 pp., \$65.00; \$29.95 (paper).

This is a useful book. It presents an up-to-date review of thinking and research dealing with personality, primarily from a psychobiological point of view. It is part of a series entitled *Problems in the Behavioral Sciences*, edited by Jeffrey Gray.

The author's preface begins with the following interesting description of his orientation:

It is not by a natural intellectual progression that one begins as a clinical psychologist in the 1950s during the era of psychoanalytic and social-environmental theory, and ends by writing a book 40 years later on the "psychobiology of personality." The first stage of evolution was an increasing skepticism of dynamic post hoc explanations of personality during my early career as a full-time clinical psychologist. Not only the study of patients, but observations of my own developing children raised questions about the adequacy of environmental explanation alone. What father can remain an adamant environmentalist after he has his second child?

The author's strategic thinking is set forth in another quotation from the first page of the text:

Sciences need systems for classifying their phenomena whether these are astronomical objects, units of matter, or species of animals. A science of astronomy that made no distinctions among planets, stars, and galaxies, a geology that regarded every rock as a unique structure, or a biology that could only distinguish two-legged from four-legged creatures, would not progress very far in understanding or prediction. Without a classification of species there could have been no *On the Origin of Species*.

The author then goes on to present a clear and satisfactory review of the literature. The chapter titles include "Basic Dimensions of Personality," "Consistency of Personality," "Behavioral Genetics and Personality Traits," "Neuropsychology," "Psychopharmacology," "Psychophysiology," "Learning," "Anxiety Disorders," "Antisocial Personality and Other Disinhibitory Disorders," and "Measures and Models, Problems and Progress." The list of references is extensive and apparently up-to-date. In addition, the author presents useful tables and figures in which he summarizes much of the important data he writes about.

I think the book could be useful as a textbook for psychol-

ogy graduate students, and a good deal of it will be of interest to psychiatry residents as well as practicing psychiatrists.

I have one specific suggestion for improving the book if it is ever revised. It would be very helpful to expand the table of contents so that the subsections of the individual chapters are listed.

Reading through the book provides the reader with a broad grasp of the field as well as an understanding of some of the important conceptual and methodological problems inherent in much of the research described.

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EATING DISORDERS

Special Problems in Managing Eating Disorders, edited by Joel Yager, M.D., Harry E. Gwirtsman, M.D., and Carole K. Edelstein, M.D. Washington, D.C., American Psychiatric Press, 1992, 237 pp., \$29.95.

Ten years ago, bulimia nervosa had just been recognized by *DSM-III*, and virtually no data were available on the management of this disorder in clinical practice or on the efficacy of specific treatment modalities. Even the more venerable literature on anorexia nervosa contained only a few rigorous studies of treatment; indeed, one analysis at that time noted that there had been no appreciable improvement in the prognosis of anorexia nervosa in the 50-year period from 1931 to 1981.

Since 1981, however, an explosion of studies has filled the literature with extensive data on the treatment of eating disorders and the many disorders that appear to occur comorbidly with them. Already this literature has become far too extensive for all but the specialist to follow. Thus, Yager, Gwirtsman, and Edelstein have performed a valuable service by attempting to condense much of this information into a small volume specifically designed to offer concrete help to the practicing clinician.

Most of the book's chapters address the numerous conditions that may occur comorbidly with eating disorders. These include psychiatric disorders, such as substance abuse, major mood disorders, and personality disorders; independent medical conditions, such as pregnancy and diabetes mellitus; and medical complications of the eating disorders themselves, including problems brought on by the abuse of laxatives and emetics. In each of these areas, the contributors not only assemble the available literature but also provide extensive case examples from their own practices to illustrate practical problems encountered in actual clinical situations. Despite the delays often inherent in assembling a multi-authored book of this type, the chapters all manage to be quite up-to-date in their coverage of the literature—an important attribute in a field with such a rapid expansion of knowledge.

I particularly recommend several chapters that assemble in a single place material rarely so well summarized before. For example, Arnold Andersen's piece on males with eating disorders is a particularly useful overview of this special topic. The chapter on laxative and emetic abuse brings together more information on this important aspect of eating disorders than I have previously seen in one place. And the final chapter, on the management of chronic and recalcitrant cases of eating disorders, provides guidelines in an area that is too rarely addressed.

In short, clinicians who regularly treat patients with eating

disorders will find this an invaluable reference. In 2 or 3 hours of reading they will gain an overview of a massive and rapidly growing literature as well as concrete, useful information on how to handle their patients.

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PSYCHE AND SOMA

Current Concepts of Somatization, edited by Laurence J. Kirmayer, M.D., F.R.C.P.(C), and James M. Robbins, Ph.D. Washington, D.C., American Psychiatric Press, 1991, 225 pp., \$31.50.

Somatization may be defined as the phenomenon by which psychological distress is expressed in somatic language and behavior and, as such, serves in many cultures as the predominant mode of affective communication. The complex process by which affective distress is communicated in somatic terms may be influenced by a multiplicity of genetic, cultural, developmental, interpersonal, and cognitive factors, and this volume examines the phenomenon of somatization from a variety of perspectives. Although a unitary theory to explain somatization is not yet possible, the editors provide multiple viewpoints on the subject and attempt to integrate them where possible. For example, from the standpoint of cognitive psychology, Pennebaker and Watson discuss the role of perception and selective attention to somatic stimuli in individual differences in reporting dysphoric states. Gregory Simon examines the relationship between somatization and the burden it places on health care utilization. He uses the population-based epidemiologic approach derived from the National Institute of Mental Health Epidemiologic Catchment Area project to analyze clusters of somatic symptoms in community samples and argues that patterns of somatization are common in the general community and only a relatively small percentage of subjects fall within the framework of what would traditionally be considered psychopathological. Other chapters review the relationship between somatization and anxiety and depression (including "masked" forms of psychiatric illness) and manifestations of somatization in primary care settings. Ford and Parker review the clinical aspects of somatization in consultation-liaison settings, particularly the role of medical-psychiatric units in the treatment of somatization-spectrum disorders. Although Kellner specifically addresses the literature on treatment, it becomes readily apparent that evaluating the efficacy of reported interventions for somatization syndromes is confounded by the lack of controlled studies as well as the lack of standardized diagnostic criteria for subject selection. The more or less "discrete," relatively common somatic syndromes encountered at the medical-psychiatric interface (fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome) are also examined in an excellent and comprehensive review by the editors.

If the text has a weakness, it may be the lack of an extensive discussion of developmental affective psycholinguistics, that is, the process by which the words of somatic language (somatothymic language) are differentiated into more abstract psychological word-symbols by cultural, developmental, familial, and learning factors. In this regard, the concept of alexithymia is given insufficient attention. Discussion of Kleinman's classic anthropological work on somatization could

also have been expanded, particularly his landmark study of neurasthenia in China.

This text provides a compact review of clinical and research aspects of the phenomenon of somatization. It is the best consolidation of the available literature since Charles Ford's *The Somatizing Disorders* (1). As a concise and timely review of the available literature, *Current Concepts of Somatization* serves its purpose well in providing a multidimensional approach to the subject that should be useful to clinicians in both medicine and psychiatry who are interested in the various forms and transformations of somatization in human behavior.

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ALAN STOUDEMIRE, M.D.
Atlanta, Ga.

From Paralysis to Fatigue: A History of Psychosomatic Illness in the Modern Era, by Edward Shorter. New York, Free Press, 1991, 419 pp., \$24.95.

This is a history of imaginary sickness written by a historian of medicine. It details the vicissitudes of somatic manifestations of psychological disequilibrium from the late nineteenth century into the present with occasional more antique references to the sixteenth and seventeenth centuries. A substantial part of the text consists of vignettes otherwise not easily accessible, translated from original sources. These vignettes can be of great value as historical referents for teaching on somatiform and psychosomatic illness.

The book is divided into large sections that chronicle the changes in the ways psychogenic sickness was, and is, manifested. The author presents his view of the changing prevalent ideas of what "facts" dictate diagnosis and treatment. The book starts with addressing the phenomenon of "psychogenic symptoms" and the nineteenth-century views of illness. The author clearly wishes to acquaint the uninitiated regarding the existence and "strength" of the unconscious force. Each chapter addresses within a temporal framework the historic ideas regarding the mysterious origins of what Freud called the "leap." Two chapters describe nineteenth-century somatic views, involving "spinal irritation" and a related but different view regarding "reflex theory." Both of these "theories" were directed toward symptoms emerging from some predisposition of the nervous system or the affected organ. The author states that such etiologies provided a "face saving fig leaf . . . for [hysterical manifestations], so that it is almost a shame [such diagnoses] were discredited." This somewhat confused metaphor conveys a pervasive view of the author—that although the origin for such illness manifestation did not belong exclusively within the body space, the later general acceptance of psychoanalytic ideas regarding etiology shamed the somatizing patient. Patients find somatic explanation for somatic difficulties far more acceptable, even if the price paid is surgical mutilation.

Such a surgical approach, as espoused by physicians for cure of, for example, "pelvic madness," led to "Battey's operation" (ovariotomy) for "nymphomania" and "hystero-epilepsy." Such "Battey-izing" and other "gynecologic tinkering" continued until late into the nineteenth century. (We know, also, that it certainly has continued in different guise even into the

present.) Women frequently asked for removal of their ovaries or clitoris (the latter by surgery or cautery or caustics) as cure for excessive sexual preoccupations or "irritability." So severe was the implicit general moral sanction and deprecation of women that the desire for such surgery by some women was also to be viewed as a psychosomatic symptom. Nor did psychiatrists at that time help. Many of the psychiatrists urged the use of gynecology in the asylums "primarily on the ground that the insane woman has as much right to be treated for bodily disease . . . as her sane sister." This was the usual conflating of seeming moral concern for the "weak" with their subjugation. This is also a contemporary battle; current views often politically and legally place one sex in the position of the inferior (1). We are told that Charcot's student Georges Gilles de la Tourette labeled such operations as "absolutely wrong."

Subsequent chapters trace the rise of motor hysteria (or hysterical paralysis) and dissociation and related phenomena, with surprising information on the frequency of catalepsy and somnambulism. Charcot is fittingly accorded a chapter with interesting biographical information and gossip on his life. It is noted that Charcot believed in somatic origins for *la grande hystérie* early and only later in life saw it as *maladie mentale*.

Later chapters encounter the gradual shift toward the concept of a cause for nervous disease in the nervous system, starting with central theories for neurosis and psychosis. The forerunner of a "psychologic paradigm" was seen in the 1880s, although earlier commentators on the human condition had made such statements far back in human history. (Epictetus announced centuries before that humankind's fantasies "alarm and disturb" more than the facts.) Psychotherapies for somatizing patients often included solace and acknowledgment of the patient's burden accompanied by placebo—as if there were, in fact, a somatic origin for the somatic symptom. Psychoanalysis is, in contrast, presented as oppression, not quite equal to that imposed by gynecologists for the same ailments. Psychoanalysts are presented as "hijacking the psychotherapies . . . [and grabbing] control of the other budding psychotherapies," and, for patients, "instilling a horror at the prospects of psychotherapy."

The important contemporary symptoms of neuromyasthenia (later called "chronic fatigue syndrome") and the Epstein-Barr virus as etiologic are addressed. The specialized reader will not find much in the way of clinically relevant summaries but more about shifting ideas and the personalities involved. The author is a historian, not a physician, and it is best to approach this volume with that understanding. The clinical specialist in this field may otherwise experience some impatience. The index is weak, omitting important entries that are in the text (S. Weir Mitchell, for example). There are phrases intended for the reader with only rudimentary medical knowledge (here is one small example: "bacteria" as the cause of syphilis rather than *Spirochaeta*). There is a lack of textured differentiation and also contradictions to what psychiatrists understand about somatic presentations. There is no reference to *DSM-III*. Psychoanalysis is deeply criticized with what seems like a superficial presentation of its theory, technique, intent, and change with time. There are places where concepts (for example, the unconscious) are reified or treated in a way that is too simplified for those of us who use the ideas as a second nature: "Given the reluctance of the unconscious to be made a fool of, patients have always tended to reject psychological interpretations of physical symptoms." Psychiatrists usually do not talk that way, at least to each other. When we read on those subjects we know about, we expect a large synthesis, new data, or a novel way of looking at things. The novelty of this book, for psychiatrists, is that it presents pri-

marily a historical, not a clinical, nosologic framework. Physicians can make best use of it by suspending some critical judgment.

This book presents more a developmental synthesis of cultural ideas regarding an important aspect of diversity surrounding sickness than a history of psychiatric treatment. Shorter keeps a fine edge on his criticism of the injustice visited on the patient by society and more proximally by the doctor. Although past and current physicians are not uniformly ignorant, venal, or brutal, this history reminds us that our actions individually and collectively can be so categorized. We can learn or, better, continuously relearn to shun a sense of absolute certainty and to cherish our tolerance for ambiguity as our natural state. Toward that purpose this scholarly historical reprise is valuable. And even if we care little about history's judgment we do care about our patients.

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Boston, Mass.

CHILDREN

Children With Conduct Disorders: A Psychotherapy Manual, by Paulina Kernberg and Saralea E. Chazan. New York, Basic Books, 1991, 297 pp., \$27.95.

The focus of this book is on the treatment of children with conduct and oppositional disorders. The book is designed to provide a treatment manual that will be of use to both clinicians and researchers. The conceptual framework draws primarily on ego analytic, object relations theory supplemented by concepts drawn from attachment, temperament, learning, and group dynamic approaches.

The book is organized into three parts covering three separate but interrelated therapy techniques. The treatments address significant influences that contribute to conduct disorder and disruptive behavior, namely, processes within the child, parent-child interactions, and peer processes and relations. The three treatments are supportive-expressive play therapy, parent training, and play group therapy. Each therapy is described with its own chapters that cover separate phases (initiation, continuation, and termination) of treatment. For each phase of treatment, fundamental processes and specific strategies are described. How the principles and strategies are to be applied concretely are well illustrated with sample therapist statements, dialogue and interchanges with patients, and case material. Thus, the book at once integrates theory and practice in a way that is clear, well organized, and thoughtfully presented.

The virtues of the book can be better seen in the context of child and adolescent psychotherapy more generally. The vast majority of psychotherapy techniques for children and adolescents currently in use (more than 230) have never been subjected to empirical research (1). Regrettably, the path from development of treatment to use and dissemination of psychotherapy does not require investigation. In the development of treatment, a critical element is specification of treatment in such a way that key elements are made explicit so that the treatment can be evaluated. Several treatment manuals are

now available for child and adolescent therapies involving psychodynamic, psychoanalytic, behavior, cognitive, and family therapies. This book adds to the store of available treatment manuals. Development of treatment manuals is not an end in itself. Rather, this is a step toward evaluation and clinical trials of the effectiveness and bases of treatment. The present book is rich in delineating procedures, strategies, and processes that can be subject to empirical test. It remains for our field to test the claims directly. In advance of the data, the authors are to be credited with moving supportive therapy, parent training, and play group therapy closer to the empirical arena.

Some weaknesses can be identified. Assessment methods to decide what treatment to provide to whom, how to evaluate whether therapeutic change has occurred to address psychodynamic conflicts central to each approach, and how to assess the processes thought to carry the burden of therapeutic change are not covered. These weaknesses are significant in relation to the next step for research but worth deemphasizing in deference to the contribution represented by the "manualization" of the treatments in this book.

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ALAN E. KAZDIN, PH.D.
New Haven, Conn.

Clinical Guide to Depression in Children and Adolescents, edited by Mohammad Shafii, M.D., and Sharon Lee Shafii, R.N., B.S.N. Washington, D.C., American Psychiatric Press, 1992, 294 pp., \$38.00.

The appearance of this multi-authored book on the clinical management and treatment of depression in children and adolescents should be viewed against a historical background. Just two decades ago, the conventional belief was that children did not get depressed or, if they did, it was masked. Epidemiologic studies of adults have consistently demonstrated that the average age at first onset of depression is often in adolescence, that prepubertal onset of depression, although infrequent, does occur, and that there has been an increase in the rates of depression worldwide in study groups born since World War II and that the average age at onset has decreased. Clinical studies show that depression in children and adolescents is associated with high morbidity. Although the last decade has witnessed an increasing amount of systematic research on depression in children and adolescents, the empirical basis for treatment is far behind that of adult depression.

This book attempts to collect the most current research on the epidemiology, neurobiology, phenomenology, and treatment of depression of children and adolescents and to present it in a form that is of use to the clinician. Due to the paucity of information, the authors have often had to extrapolate from studies of depressed adults. A revision of this book will be needed in several years to include more recent studies of the offspring of depressed parents, the adaptations of short-term adult psychotherapies to the treatment of adolescents, and the studies of depressed children who have grown up. In the meantime, this is an excellent review, written in a readable but well-referenced fashion, that should be of use to clinicians as well as new investigators wanting to learn about the field.

The chapter on the pharmacological treatment of depres-

sion is particularly useful. It summarizes the primarily negative studies so far, discusses the methodologic problems, and gives a reasonable clinical guide to the use of pharmacotherapy. The two chapters on individual psychotherapy, dynamic psychotherapy, and cognitive therapy need to rely on clinical experience alone because there had not been any published controlled clinical trials of any individual psychotherapy in depressed children or adolescents. Fortunately, manuals are being developed for cognitive and interpersonal psychotherapy, and studies are in the planning phases. There have been some recent trials on group approaches to the treatment of depressed adolescents, but these are not included in the chapter on group psychotherapy. A future revision of this book will definitely be needed in this area in a few years. The chapters on bipolar disorder are excellent synopses of the state of understanding done by investigators who are active researchers in this area.

In summary, this is a well-written, useful, and, for the most part, empirically based clinical guide in an area of public health importance.

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FREUDIAN CLASSICS

On Freud's "Analysis Terminable and Interminable," edited by Joseph Sandler, Ethel Spector Person, and Peter Fonagy for the International Psychoanalytical Association. New Haven, Conn., Yale University Press, 1991, 162 pp., \$22.50.

This slender volume represents the first in a new series entitled Contemporary Freud: Turning Points and Critical Issues, which proposes in each volume to present one of Freud's classic papers followed by commentary by a number of psychoanalysts from different countries and with different theoretical perspectives. (I have already read the second book in this series, which deals with "On Narcissism: An Introduction" [1], and can attest that it is wonderful.) The present volume, which is not quite as illuminating as the second volume in the series, concerns the masterpiece "Analysis Terminable and Interminable," published in 1937 when Freud was 81 years old, a truly remarkable work by a man of any age, and made more remarkable by the advanced age of its author.

Years ago, one could assume that everyone reading this review would be familiar with this famous paper, but I regret to say that, as a function of the change in what is taught in psychiatric residency programs today, this assumption can no longer be made. To anyone who is interested in doing psychotherapy, this paper by Freud is an absolute classic and required for reading and study. It has many highly controversial statements and has often been called pessimistic, but it is remarkable for its calm and clearheaded realism and for its prescience in raising a number of issues that became increasingly important after Freud's death.

Somewhat loosely organized, Freud's paper purports to be a clinical study but actually contains many overt and covert controversial metapsychological assumptions. It deals primarily with the limitations of psychoanalysis. The editors tell us that, for Freud, "the outcome of treatment is ultimately constricted by 1) the constitutionally determined intensity of the patient's drives, 2) the severity of infantile traumas, and 3) the degree of ego distortion produced by defenses" (p. x). Among these resistances to recovery, Freud discussed certain "altera-

tions" in the ego that in turn are selected on the basis of factors determined by inherited and cultural dispositions. These alterations are effects brought about in the ego by the defenses and by certain constitutional factors, such as adhesiveness of the libido, too mobile a libido, depletion of plasticity and capacity for change, and an ultimate force toward suffering involving guilt, the need for punishment, and the death instinct. Some of these metapsychological concepts are outmoded today, and the paper includes a somewhat difficult mixture of Freud's topographic and structural theories.

Freud also focuses on the analyst and his or her role in the success or failure of the treatment. He points out that analysts do not always come up to par as models of normality, teachers, and persons with a love of truth that "precludes any kind of sham or deceit" (p. 35). This leads to Freud's famous statement that psychoanalysis along with education and government is an "impossible" profession.

The discussions in the volume range over a wide area of topics, some of which are quite abstruse, and in the present review I will touch on only some points that may be of interest to psychiatrists. Arlow points out the inconsistencies in the two models used in the paper: "Whereas the topographic model stressed the pathogenic significance of what was repressed into the system *Ucs*, the structural model stressed the role of intrapsychic conflict and compromise formation" (p. 43). Arlow points out that undoing repression, for example by recollecting forgotten memories, is no longer the crucial aim of psychoanalytic technique, although Freud in this essay concentrated on it as crucial. Arlow offers an update of Freud's approach in the light of ego psychology and the structural theory as well as some of his own ideas about unconscious fantasies. Thus, the analysis of compromise formations, especially those which are ineffective and pathogenic, becomes the central technical issue rather than the uncovering of the repressed. Arlow offers a number of other emendations and corrections of Freud's paper without detracting from the greatness of this classic work. To those interested in the whole topic of how psychoanalytic treatment works, Arlow's commentary is required reading along with Freud's paper, as long as one remembers that some of Arlow's contentions also remain controversial.

The volume would have been improved if Arlow's "traditional" paper had been followed by a discussion written by a self psychologist such as Muslin (2). However, I fear that some psychiatrists will become lost in at least a little of the published discussion that actually follows in the volume, because it becomes at times quite abstruse and occasionally assumes some highly technical theoretical knowledge of metapsychology and of disagreements at a metapsychological level among psychoanalysts. There is also considerable discussion of historical detail surrounding the composition of this paper, which may be of interest but is not of primarily practical importance.

There are some further useful emendations, however. Zimmermann and Mostardeiro divide Freud's paper up by the topics covered and comment lucidly and in a clinical manner on each. These topics include the duration of the analysis, assessing the readiness to terminate, the constitutional strength of the drives, protection against further psychic conflict, alterations in ego structure, the personality of the analyst, and issues involving femininity. In general, Zimmermann and Mostardeiro seem more accepting of Freud's position than Arlow, and their conclusions (pp. 90-91) have valuable clinical content and should be studied carefully.

A Kleinian discussion of some of the subthemes of the paper is offered by de Folch. Cooper wisely challenges what is probably the weakest part of Freud's paper, namely, his notions of

masculinity, femininity, and of what constitutes the "bed-rock" of analysis. Very few analysts agree with Freud's views on these topics today.

The remarkably wide range of the discussions stirred up by Freud's paper illustrates its fertility and importance to anyone who would practice psychotherapy. For those who are not familiar with Freud's paper, this book is an excellent starting point because it begins with a reprint of the paper. For those who are familiar with the paper, there is something for every kind of interest in the discussions that follow it, and I can recommend the book highly. The primary audience for this book are psychoanalysts, and those psychiatrists who are not psychoanalytically oriented will not appreciate the topics covered in it. I have discussed my own views on some of these issues elsewhere (3, 4), and the *International Journal of Psycho-Analysis*, volume 68, part 1, 1987, contains three more papers on Freud's classic that should be read along with this book.

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Freud's "On Narcissism: An Introduction," edited by Joseph Sandler, Ethel Spector Person, and Peter Fonagy for the International Psychoanalytical Association. New Haven, Conn., Yale University Press, 1991, 227 pp., \$27.50.

Almost 80 years have passed since Sigmund Freud introduced the term "narcissism" into the language of psychiatry, transforming it from the designation of an obscure sexual deviation to a broad general concept with major implications for theories of normal development, psychopathology, and psychoanalytic therapy. Like many of his landmark essays, "On Narcissism: An Introduction," published in 1914, has been reconsidered and reinterpreted repeatedly as psychoanalytic theory has evolved and has been applied to a broad range of clinical problems and issues in the social sciences (e.g.,

Christopher Lasch's *The Culture of Narcissism* [1]). Many readers have found the paper heavy going; in covering so broad a terrain it left many stones unturned and boundaries uncertain.

As one of its continuing series of volumes on Contemporary Freud: Turning Points and Critical Issues, the International Psychoanalytical Association has organized this symposium, opening with a reprinting of Freud's essay and following it with a set of commentaries, critiques, and updatings by an international group of psychoanalysts representing the spectrum of current viewpoints within the widening mainstream of analysis in the 1990s.

Clifford Yorke's "teaching text" is particularly valuable in pointing up the areas of semantic unclarity and conceptual transition that mark Freud's attempt to bring his new clinical observations into line with the increasingly shaky edifice of the libido theory, then under assault by Adler and Jung. Otto Kernberg offers a "contemporary reading," presenting in brief his effort to synthesize an object relations perspective with traditional drive theory, and Paul Ornstein presents a lucid distillation and defense of Kohut's revisionist views that, emerging from his observations of narcissistic transference, have evolved into a "self psychology" which challenges classical conflict theory. Hannah Segal and David Bell contribute a particularly clear statement of the contemporary Kleinian viewpoint, challenging Freud's notion of "primary narcissism" in favor of the thesis that object relations are present from the moment of birth. Indeed, Bela Grunberger, a French analyst, would trace psychic life to the intrauterine period and considers narcissistic phenomena to be regressive expressions of—at least fleeting—unconscious memories of fetal life.

Other contributors, less known to American psychiatric readers, bring perspectives from European and Latin American psychoanalysis that enlarge upon but do not fundamentally conflict with these more familiar views. Together they develop a wide-ranging exegesis of a complex problem that Freud bequeathed to posterity with this provocative but often puzzling paper. The editors have performed a valuable service by underscoring the epistemological and clinical issues that Freud left unresolved and by bringing together a group of thoughtful efforts to engage and clarify them. For those who have long struggled with "On Narcissism," this volume may prove a useful guide to the perplexed.

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Reprints of Book Forum reviews are not available.

Sudden Self-Harm While Taking Fluoxetine

SIR: We would like to report a case in which a patient taking fluoxetine was suddenly overcome by the urge to do himself harm.

Mr. A, a 44-year-old man with chronic depression, mixed symptoms, was treated in a double-blind trial of nefazodone, fluoxetine, or placebo. Clinical features included sadness, dysphoria, and repressed irritability; some compulsive counting, showering, and cleaning; and passive suicidal ideation. These features showed a mild seasonal pattern. He kept to himself to preclude arguments or lashing out. His occupational performance was unimpaired by depression, but his social life was significantly curtailed. His wife said he was verbally, but not physically, abusive to his children.

Mr. A had abused alcohol 25 years earlier during a previous episode of depression; he experienced limited symptom anxiety attacks during the current episode. Alcoholism was present in both maternal and paternal relatives, a paternal aunt committed suicide, and a paternal uncle was "psychotic." His childhood history revealed poor concentration, nervousness, inattention, shyness, impersistence, and dyslexia and "learning disabilities." Thus, he may have suffered attention deficit disorder in childhood. Although he was physically abused by his father as a child, he had no documented history of head injury or neurologic disease.

On a previous trial of fluoxetine, 60 mg/day, he noted better mood, followed by irritability, mood lability, and other symptoms consistent with either mild hypomania or agitation. His previous irritable and abusive behavior was probably symptomatic of a mixed mood disorder rather than borderline personality disorder.

Mr. A failed to respond to an 8-week trial of what was later identified as nefazodone and was crossed over to what was later identified as fluoxetine. He responded partially (17-item Hamilton Rating Scale for Depression score decreased from 24 to 10) after 10 weeks on a regimen of fluoxetine, 40 mg/day. At 12 weeks he felt mounting tension and an increase in depressive symptoms following subjective work stress. We assumed lack of efficacy and increased the dose to three capsules (later identified as fluoxetine, 60 mg/day). The patient mistakenly increased the dose to 80 mg/day. Twenty-four hours after the 80-mg dose, he impulsively made superficial cuts to his throat, wrist, and abdomen while driving, with the express purpose of cutting but not killing himself. This compulsion was accompanied by relief but not pain. He had never had the urge to cut himself before. Within 48 hours (160-mg additional dose), he suffered disturbing nightmares, best remembered as "I'm being hurt."

The patient decreased the dose to 20 mg/day. Within 24 hours the urge to cut himself had disappeared, and within 48 hours the disturbing nightmares had stopped. After 1 week of 20 mg/day dosing he noted clear loss of drug efficacy (17-item Hamilton depression scale score was 16), and the research trial was terminated. The code was broken and

study drug number 2 was identified as fluoxetine. The adverse events appeared directly related to the dose of the study drug.

Desipramine, 150 mg/day, led to a significant decrease in depressive symptoms, but no return of nightmares or urge to cut himself. Mr. A's sour disposition and irritability remained.

Like many of the original cases reported by Teicher et al. (1), this man may have had a CNS abnormality. No EEG or imaging studies were performed. Downs et al. (2) have suggested that "obsessive-like, violent thoughts of suicide will occur in patients with some form of limbic system dysfunction." This case demonstrates a prior possible hypomanic response to fluoxetine (3) and a dose-related, irresistible impulse to cut but not kill oneself. The sudden urge to cut appears related to dose but not antidepressant effect, so it may be due to an intolerable agitation rather than a switch to mania.

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Fluoxetine-Induced Anorexia in a Bulimic Patient

SIR: Fluoxetine treatment for bulimia nervosa has been recently reviewed, suggesting its efficacy in this eating disorder (1). We report a case of a bulimic patient in which fluoxetine reversed both eating binges and vomiting but then resulted in restricted food intake, altered body image, and amenorrhea.

Ms. A, a 22-year-old woman, was 168 cm tall and weighed 56 kg. She had no previous psychiatric history. Two years prior to presenting for treatment she gradually began to experience episodes of increased appetite, with markedly increased food intake. She began to be concerned about her weight gain and would induce vomiting following each binge. The episodes increased in frequency and were associated with increasing anxiety that was relieved only by eating binges. She became irritable, impulsive, and increasingly depressed. Her social and familial relationships seriously deteriorated. Physical and laboratory examinations revealed no significant abnormalities, and there was no history of menstrual irregularity.

After the diagnosis of bulimia was established, Ms. A received fluoxetine, 20 mg/day, and weekly supportive psychotherapy. During the first month the dose was increased

gradually because of continued symptoms. One week after a 60 mg/day dose was reached, the frequency of eating binges and vomiting began to decrease. After 3 weeks, bulimic symptoms had almost completely disappeared and the patient was euthymic. One month after treatment at this dosage the patient developed amenorrhea and a preoccupation with weight gain; she began to restrict severely her caloric intake. Fluoxetine had to be discontinued when the patient's weight fell below 50 kg. One month later, bulimic symptoms recurred, the patient's weight increased, and the amenorrhea, as well as other anorexic signs, gradually disappeared.

It has been proposed that the abnormal eating patterns that characterize bulimia nervosa could result from an imbalance between facilitatory α -noradrenergic and inhibitory serotonergic pathways (2). Thus, drugs that potentiate 5-hydroxytryptamine (5-HT) activity may reduce bulimic symptoms. Some authors have proposed that these drugs might induce anorexia through a stimulation of 5-HT_{1D} receptors (3), which could enhance satiety (4). Although the neurobiology of anorexia nervosa still remains poorly understood, a serotonergic hyperactivity has been suggested to play a role. This could explain the appetite stimulant effect of 5-HT antagonists such as cyproheptadine (5). This hypothesis would place bulimia nervosa and anorexia nervosa on opposite poles of a clinical and pathophysiologic continuum.

To our knowledge, there are no reports of a fluoxetine-induced anorexia nervosa-like syndrome in a bulimic patient. The case reported here illustrates the potential importance of the serotonergic system in eating disorders and supports the possibility of inverse pathophysiologic pathways between bulimia and anorexia nervosa. This case may also highlight the possible adverse effect of 5-HT reuptake inhibitors when used in bulimic patients.

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Lyell Syndrome and Lethal Catatonia: A Case for ECT

SIR: We would like to present the following case report.

Ms. A, a 43-year-old woman with a history of bipolar affective psychosis, had been prescribed carbamazepine, 200 mg/day, sulpiride, 600 mg/day, and perazine, 100 mg/day, for pending exacerbation of her psychiatric illness. Fourteen days later she developed a progressive exfoliative

skin disorder with multiple painless blisters of the face, trunk, arms, and mucosal surfaces of the mouth, eyes, and vulva. The patient was admitted to the local dermatology clinic and given a diagnosis of Lyell syndrome (toxic epidermal necrolysis), a rare severe toxic reaction to different drugs, including carbamazepine, characterized by epidermal blistering and peeling of the skin in large sheets (1). All psychotropic medication was withdrawn. High doses of steroid therapy (initial dose, methylprednisolone, 250 mg/day) and supportive care were administered. After a few days Ms. A exhibited mixed bipolar disorder with mood-congruent psychotic features (*DSM-III-R*) that progressed rapidly to full-blown lethal catatonia (2), a rare life-threatening disorder of psychomotor disturbances and autonomic dysregulation. The patient was given six unilateral ECT treatments within 2 weeks and showed a remission of lethal catatonia within hours and a remission of the affective syndrome within 2 weeks. Steroids were tapered quickly and the skin lesions disappeared within 4 weeks.

ECT is an effective and safe treatment for lethal catatonia (2), even in high-risk patients. Carbamazepine was the drug most likely responsible for Lyell syndrome in our patient, but we were nevertheless reluctant to administer other neuroleptic drugs, which are also less effective in lethal catatonia than ECT. Steroid therapy may cause affective and paranoid psychoses (3), but steroid-related catatonia is apparently very rare (4). Corticosteroids were advocated as a treatment modality for lethal catatonia in the preneuroleptic era (*DSM-III-R*). Continuous steroid therapy in our patient may have blunted the syndrome of lethal catatonia initially and may have contributed to its rapid remission during ECT.

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Use of Pimozide in the Pisa Syndrome

SIR: The Pisa syndrome, a dystonic reaction that appears as a side effect of antipsychotic agents (1), is considered to be a subtype of tardive dystonia (2). It is usually difficult to treat this condition without discontinuation of antipsychotics (3). However, we report a case where the patient dramatically recovered from the Pisa syndrome following a change in medication from haloperidol to pimozide, a selective dopamine D₂ receptor agent, without any reduction in the clinical antipsychotic effects.

Mr. A, a 22-year-old man with mental retardation (IQ=44, Suzuki-Binet Test), was admitted to a psychiatric hospital with a diagnosis of schizophrenia. The patient initially received haloperidol, 9 mg/day; propicazine, 75 mg/day; and

biperiden, 3 mg/day. The dose of haloperidol was gradually increased to 27 mg/day and propericiazine to 225 mg/day over the next 4 weeks. Within the following week, Mr. A's trunk gradually developed a peculiar position, with side flexion of the body and backward axial rotation. The patient was considered to be suffering from the Pisa syndrome, since he fulfilled the criteria for tardive dystonia developed by Burke et al. (2) and showed the typical posture of this syndrome (1) without any other dystonic reactions.

The propericiazine was first discontinued, and then haloperidol was decreased to 18 mg/day over 4 weeks, but without any noticeable improvement. We then tried agents reported to improve tardive dystonia, such as promethazine, amantadine, tiapride, carbamazepine, and dantrolene sodium. Each of these was prescribed for more than 2 weeks with no benefit. Finally, we changed the patient's antipsychotic from haloperidol, 18 mg/day, to pimozide, 18 mg/day. From that time on, the dystonic symptoms gradually improved and almost completely disappeared within 1 week. The symptoms did not recur over the next several months.

We changed the antipsychotic agent for the following reason. There has been no report of selective D₂ antagonists causing the Pisa syndrome. The affinity of pimozide for D₂ receptors is higher than that of haloperidol in *in vitro* radioreceptor assay (4). This suggested that the activity of haloperidol at non-D₂ receptor sites may be responsible for the syndrome. For example, blockade of the sigma receptor, which haloperidol exhibits with a high affinity, is considered to play a role in dystonia (5).

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Rare Presentation of Tardive Dyskinesia

SIR: Severe presentations of tardive dyskinesia (1) are frequently disabling because of difficulties in masticatory movements, severe tardive akathisia, or limb and finger movements. Respiratory or swallowing dyskinesias producing irregular respiratory rates or grunting noises have been

rarely reported (2). Therapeutic strategies, often irrelevant in treatment, are more difficult and ineffective in these cases (1). We observed a case of rare and severe presentation of tardive dyskinesia in a 57-year-old woman with a diagnosis of dysthymic disorder and histrionic personality disorder according to *DSM-III-R*.

Ms. A had been treated for several years with high potency neuroleptics, probably to contain agitation and anxiety unresponsive to benzodiazepines. Persistent tardive dyskinesia was diagnosed according to Schooler and Kane criteria (3) using the Rockland Simpson scale for tardive dyskinesia (4). Ms. A's total score was 48.

Upon admission Ms. A showed chewing movements, choreoathetoid movements of the tongue, blepharospasm, finger movements, akathisia, and lordosis with abnormalities of gait. These signs were associated with a continuous, rhythmic, clearly involuntary vocal emission, like a cry, the origin of which seemed to be laryngeal, defined by the patient as "illness of the cry."

The vocal emission (together with other signs) followed typical tardive dyskinesia patterns, disappearing only during sleep and worsening with anxiety, and its continuous occurrence affected severely the patient's speech and ability to fall asleep. Awareness of this symptom was higher than for the other symptoms, maybe because of the auditory feedback. During 2 years of illness, severity was reported to decrease if neuroleptic doses were increased and to worsen upon decrease or withdrawal. The severity also increased if anticholinergics were used. In the last 6 months severity was stable with Ms. A taking clothiapine, 40 mg/day. Withdrawal from medication induced a significant worsening of vocal emission and other symptoms.

Neurological examination and nuclear magnetic resonance imaging excluded an olivopontocerebellar syndrome, which was considered in differential diagnosis, as well as other neurological conditions possibly related to the vocal emission and other involuntary movements.

After 1 week of treatment with clonazepam, 8 mg/day, most symptoms decreased, except lordosis, gait disturbances, and the vocal emission (total Simpson scale score=38), which remained unchanged throughout the following 1-month observation period.

The similarity of our patient's symptoms with Tourette's disorder is worth noting. Our observations seem to be quite similar to cases of tardive Tourette's disorder reported in the literature (5).

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Schizophrenia and Chromosomal Fragile Sites

SIR: Family, twin, and adoption studies have provided evidence that genetic factors play an important role in the etiology of schizophrenia, although no specific genetic mechanism has yet been identified. In recent years further information about the nature of the genetic effect has resulted from cytogenetic and molecular investigations. After the initial report of the cosegregation of schizophrenia with a partial trisomy of chromosome 5, linkage studies with genetic markers suggested the involvement of a susceptibility locus for this disease on the long arm of chromosome 5 (1). However, further studies did not confirm such results (2). In one survey, no chromosomal defects were found in a male schizophrenic population (3), although evidence of chromosomal fragile sites has been reported in schizophrenic patients with cutis verticis gyrata (4).

A cytogenetic investigation was carried out at a psychiatric hospital in 48 unrelated male patients, aged 28–58 years (mean=44.6 years), with chronic schizophrenia, diagnosed according to the *DSM-III-R* criteria and divided into five clinical subtypes (i.e., disorganized, paranoid, catatonic, undifferentiated, and residual). The control group consisted of 20 healthy male volunteers, aged 24–52 years (mean=37.5 years), recruited from nursing staff and physicians at the hospital. Cytogenetic analysis in blood lymphocytes, cultured by the method of Neri et al. (5) for identification of folate-sensitive fragile sites, showed a significantly higher presence of rare fragile sites in metaphases of schizophrenic patients than in the control group ($p<0.001$). The chromosomes most involved were 9 and 10, often with fragility at p21 and at q21, respectively. The fragile 9(p21) and fragile 10(q21) sites were present in 56% and 52% of patients, respectively, with a proportion of positive cells ranging from 2% to 17%, while fragility of chromosome 9 and 10 was found only in 15% and 25% of normal subjects, respectively, with a variability of expression from 1% to 6%. A lower frequency of fragile sites was observed on other chromosomes (i.e., on chromosomes 3, 8, 12, and 16). With regard to the X chromosome, the fragile site at Xq27 was detected in few cells, with no differences between patients and healthy volunteers. There was no difference in the presence of chromosomal fragility among patients of different schizophrenia subtypes.

Autosomal fragile sites have been regarded as normal variants associated with no specific clinical condition. The finding of a high frequency of fragile sites on chromosomes 9 and 10 in male schizophrenic patients indicates that fragility could have a role in the etiopathogenesis of schizophrenic disorder. Admittedly, since the fragile X site is difficult to detect in female carriers by chromosome analysis, our investigation was conducted only in male subjects and, therefore, these results need to be confirmed also in female patients. The identification of such chromosomal abnormalities associated with schizophrenia might provide important leads in the search for the chromosomal location of major genes in this disease.

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Serotonin Syndrome

SIR: Harvey Sternbach, M.D. (1), did an excellent job of summarizing the rather disparate literature on clinical and preclinical aspects of the serotonin syndrome. We would like to add to his review our own experience with this phenomenon, which we believe to be unique in that our observations were made under the controlled conditions of the laboratory.

As part of our ongoing research on serotonergic function in humans, we have been investigating the neuroendocrine and behavioral effects of intravenous L-tryptophan (L-Trp) in a number of neuropsychiatric disorders and during treatment with a number of neuropharmacological agents (2). In one of our studies (3), we administered doses of L-Trp ranging from 4.5 to 7.0 g i.v. to nine patients with major depression who were receiving treatment with the monoamine oxidase inhibitor (MAOI) tranylcypromine. In addition to observing an enhancement of the prolactin response to L-Trp during tranylcypromine treatment, presumably reflecting enhanced serotonergic function, four of our nine patients developed a distinctive neuromotor syndrome following L-Trp infusion during tranylcypromine, but not during placebo, treatment. Symptoms included hyperreflexia, ankle clonus, nystagmus, incoordination, tremor, myoclonic jerks, and nausea. There were no obvious cognitive changes or seizures. One patient with a previous history of hypomania developed elated mood and pressured speech. The full syndrome generally lasted 6–12 hours, although isolated symptoms persisted for up to 24 hours in individual patients, with complete resolution thereafter. There were no evident sequelae. There were no differences in peak prolactin, mood, or autonomic responses between patients with and without the syndrome, but those with the syndrome had received tranylcypromine for a shorter period of time (mean=8.3 days, SD=4) than those without the syndrome (mean=22.6 days, SD=5.4).

Interestingly, in similar studies using the L-Trp infusion to assess the serotonergic effects of the selective and potent serotonin reuptake inhibitor fluvoxamine (4), we saw little of the full-blown syndrome described above, although a few patients developed some isolated myoclonic jerking.

Our findings suggest that the ability of a drug to induce the serotonin syndrome in humans depends not only on its ability to enhance potentially serotonergic function but also on the mechanism by which it effects that enhancement. MAOIs may have

a particular propensity for inducing the syndrome, especially early in treatment, before compensatory mechanisms have come into play. With the increasing availability and utilization of drugs with potent effects on serotonergic systems, we agree with Dr. Sternbach that increased vigilance for these adverse effects is critical.

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The (Ab)use of Computers

SIR: Computers facilitate the collection, organization, and manipulation of data from large numbers of patients and have great value for clinical, research, and administrative tasks (1, 2). However, computers can be abused and mislead us. Several obvious errors in our computerized data base led to a process of reviewing data prior to computer entry which, in turn, identified other less obvious, but serious, pitfalls of computerizing unreviewed data.

After a 1-hour orientation to the use of an optically scannable patient consultation record (1), residents and fellows used it to record data on all patients seen by our medical center consultation/liaison service. At the end of each consultation, the patient consultation record and a copy of the initial consultation note were reviewed by a senior attending physician before the patient consultation record was scanned for data entry. Incomplete or inaccurate patient consultation records were returned by the reviewer to the trainees for correction and re-review. After noting a high number of inaccurate forms returned, we systematically collected data on rates and types of patient consultation record errors for a 10-month period. There was a token incentive (a free monthly lunch) for the trainee with the highest rate of initially accurately completed patient consultation records.

The monthly rate of accurate completion ranged from 0% by a resident in his first month of rotation to 86% by a fellow in his sixth month. Overall, during the period of the review, 50% of the patient consultation records initially had at least one error, with half of the rejects having more than one error. When rejected patient consultation records were reviewed for type of error, 50% had missing data, 33% factual errors, and 58% errors of interpretation.

In addition to providing more accurate data, close review of the forms prior to computer entry offers an opportunity to evaluate and improve trainee performance. A trainee's accuracy of patient consultation record completion seemed to par-

allel his or her clinical performance on the consultation-liaison rotation, i.e., inaccurate completers were poor performers and vice versa. Record accuracy problems often alerted us to trainee needs for specific teaching interventions. Finally, the elimination of incomplete forms by review enabled us to identify a mechanical problem with the optical scanner. When the computer printout indicated a large number of forms with no data for a particular item, our knowledge that such incomplete forms were not entered led to a speedy correction of the hardware problem.

We remain enthusiastic about the many uses of computers in a psychiatric setting, but our experience confirms the well-known motto of the computer industry, "Garbage In, Garbage Out." In addition to computer checks for completeness, we strongly recommend professional reliability review of all clinical data prior to computerization.

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MARY ALICE O'DOWD, M.D.
F. PATRICK MCKEGNEY, M.D.
Bronx, N.Y.

Alcohol and Addictions

SIR: I enjoyed reading the overview of substance abuse disorders written by the Group for the Advancement of Psychiatry (GAP) Committee on Alcoholism and the Addictions (1). I would, though, like to make two points.

When the authors discussed the treatment of substance abusers, the goal of abstinence was strongly suggested. While the feasibility of controlled drinking was discussed, and it was mentioned that certain patients can achieve a stable recovery with controlled drinking, controlled drinking was essentially portrayed as doomed to fail. Consequently, at the outset of treatment, it was suggested that the goal of abstinence should be conveyed to all patients. There are, however, considerable data that support controlled drinking as a viable treatment goal (2). In addition, whether or not moderation of drinking will be successful, it can frequently be critical at the outset of treatment to develop a controlled drinking contract with patients who want to try this approach so that they can discover for themselves whether controlled drinking is possible for them. If moderating drinking proves unsuccessful, then abstinence should be considered. In my experience, denial, if it is operating, can frequently be broached by this method rather than by insisting on abstinence at the start of treatment.

The second point concerns self-help organizations. The authors discuss Alcoholics Anonymous (AA), which is an important, if not sometimes essential, treatment modality. They also mentioned Narcotics, Gamblers, Pills, Cocaine, Drugs, and Overeaters Anonymous. There are, however, two other self-help organizations designed to be of help to the substance abuser that were not mentioned: Rational Recovery and Secular Organizations for Sobriety. For patients who cannot connect with AA or other similar programs, these organizations should be suggested. Their philosophies are strikingly different than that of AA or any of the other self-help programs based upon the philosophy of AA. Such organizations may fit

better with the character structure of some patients who find AA distasteful. There may be times when resistance to AA may not need to be "worked through"; instead, the resistance could be accepted.

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MICHAEL LEVY, PH.D.
Andover, Mass.

SIR: The recent article by the GAP Committee on Alcoholism and the Addictions "reviews the role of the psychiatrist in the evaluation and treatment of patients with substance use disorders." The review covers the major areas in assessment and treatment thought pertinent to psychiatrists. Although such a review article clearly cannot cover all the issues, we would like to note two important areas overlooked by this report.

The first is the absence of references to behavioral formulations of alcohol and drug abuse and the efficacy of behavioral therapies for these disorders. This is surprising given the utility of behavioral theories. For example, the concept that drugs can serve as reinforcers similar to food and water has been used to understand how drugs that produce little withdrawal can be drugs of dependence. This formulation has also led to effective procedures for screening new compounds for abuse liability and for examining genetic and environment factors thought to control drug use. Behavioral approaches have also produced some of the more impressive abstinence rates (1). In addition, behavioral approaches (e.g., relapse prevention) have slowly been incorporated into many different treatment approaches.

The second area overlooked is that, although alcohol, cocaine, marijuana, opioids, and other drugs are mentioned, nicotine is ignored. This stance is consistent with the absence of any mention of nicotine dependence or smoking in the recent National Consensus Standards for Postgraduate Medical Fellowship Training in Alcoholism and Drug Abuse put forward by the American Academy of Psychiatrists in Alcoholism and the Addictions (2). These absences suggest nicotine dependence is not a disorder of sufficient importance to be addressed by psychiatrists. In reality, smoking causes three times the number of deaths as all other forms of drug abuse combined, can be as intractable as other severe dependencies, and is linked to several psychiatric disorders (3).

Part of the reason behavioral approaches to drug abuse and smoking as a form of drug abuse were omitted from the GAP report may be that these are very seldom addressed in traditional alcohol/drug abuse programs (4). Even so, reports such as the GAP report should highlight issues that have been scientifically shown to be of importance but have been ignored by the current research and treatment establishments.

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JOHN R. HUGHES, M.D.
WARREN K. BICKEL, PH.D.
STEPHEN T. HIGGINS, PH.D.
Burlington, Vt.

SIR: The GAP Committee on Alcoholism and the Addictions presented an excellent overview for the general psychiatric practitioner on the substance abuse disorders. Perhaps one of the reasons for the persistent resistance of our colleagues to accept the patient with substance abuse as "one of our own" is the semantic separation we foster between the substance abuse disorders and other psychiatric disorders. The Committee notes, for example, the "high prevalence of psychiatric disorders among patients with substance abuse problems." The psychiatric disorder most common in patients with "substance abuse problems" is, in fact, a substance abuse disorder. As the medical director of a substance abuse program, I strive to teach medical students rotating through our program that they need not bemoan the absence of "real" psychiatric patients on our unit. Rather, substance abuse will likely be the most common psychiatric disorder they will come in contact with in their future medical practice. When the psychiatric community can begin to accept the substance abuse disorders as a disorder equal in weight to all other psychiatric disorders, we will have made a critical step in acknowledging our primary role in the recognition, assessment, and treatment of this patient population.

BRYON ADINOFF, M.D.
Charleston, S.C.

Dr. Khantzian Replies

SIR: Our GAP report on substance abuse disorders as a psychiatric priority struck the theme that the problem of substance abuse has been neglected or responded to insufficiently by the medical profession in general and by the psychiatric profession in particular. It is a problem that keeps eluding us, and we keep denying how basic and pervasive the problem is. At the same time, we generalize about treatments and, intentionally or inadvertently, fail to consider the subtleties of individual patient needs or the advantages of treatment approaches that are less familiar to us or compatible with our pet ideologies or theories. The three letters authored respectively by Dr. Levy, Dr. Hughes and colleagues, and Dr. Adinoff correctly and legitimately underscore that the GAP Committee on Alcoholism and the Addictions, despite our best intentions, did not cover all the bases. These letters bring to our attention basic and added important dimensions of alcoholism and addiction that should be considered.

Dr. Levy's letter raises the controversial issue of whether alcoholics can ever resume controlled drinking. There is a plethora of rigid opinions about this in the field that, in their extremes, either place patients at risk, creating unrealistic or

unachievable goals, or cause other patients to abandon treatment when an unswerving attitude about the requirement for abstinence is prematurely and insistently advocated. I personally agree with Dr. Levy and have described in the literature (1) how we can establish an alliance with our patients, usually less severe cases, in collaborating with them and testing whether controlled drinking is a possible or realistic option. I also agree with Dr. Levy that alternatives to 12-step programs such as AA are necessary. I suggest that, for some, the most important ingredient in recovery is the association and interaction with others who are recovering, which groups like Rational Recovery and Secular Organizations for Sobriety provide. Such opportunities for interaction are antidotes to the pervasive, crippling isolation and self-absorption that so powerfully perpetuates substance abuse disorders.

The letter by Dr. Hughes and colleagues rightfully points out omissions in two important areas, namely 1) overlooking behavioral formulations of substance abuse disorders and the efficacy of behavioral therapies, and 2) the failure to mention nicotine as an addictive drug. Dr. Hughes and associates are probably right that this in part reflects that behavioral approaches and nicotine addiction are seldom addressed in most substance abuse programs. Consistent with their speculation, I also know that few, if any, of us on the committee have directly worked in these areas, although most of us in retrospect would agree that both areas should have been addressed. Finally, I am also in agreement with Dr. Adinoff that the most common psychiatric disorder in patients with substance abuse problems is substance abuse disorder. A fact that keeps escaping clinicians and others is that substance abuse, as much as it is anything else, is a psychiatric condition.

Notwithstanding these omissions, I believe it was an accomplishment to bring our GAP report to fruition in the *Journal* and to reach the consensus we did as a committee. Prior to 1986 there was no GAP Committee on Alcoholism and the Addictions. At its inception we believed we could produce a position paper within a year. It took 4 years, but I am pleased and satisfied we were clear enough about what we did include and cover. We appreciate being astutely reminded by thoughtful colleagues about what else we might have covered or stated more clearly.

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EDWARD J. KHANTZIAN, M.D.
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Kleptomania and Shoplifting

SIR: Marcus J. Goldman, M.D. (1), cited our article (2) as the source for his statement that "kleptomania may account for a substantial proportion of the staggering 40 billion dollars in business losses attributed to shoplifting each year."

I wish to make two points regarding this citation. First, our article stated that "shoplifting losses in the United States have reached an annual amount of approximately 24 billion dollars" and not 40 billion. Second, we never indicated that kleptomania accounted for a "substantial proportion" of shoplifting losses. On the contrary, we stated that "[kleptomania] is, in our experience, infrequently observed" in apparently nonsensical shoplifting cases. Indeed to the current date Dr. Atcheson and I have estimated that less than 10 of the hun-

dreds of shoplifters we assessed would be considered to be suffering from this disorder.

The major findings of our initial clinical research regarding the underlying causative factors in those apparently nonsensical cases of shoplifting that we assessed, clearly indicated that they were most definitely *not* of the kleptomania type, differing on virtually all the DSM criteria for kleptomania quoted by Dr. Goldman.

Furthermore, our cited article, in fact, indicated in the vast majority of the cases that we assessed from 1979 to 1982 (and, incidentally, our later clinical assessments have strongly supported these earlier findings), that at psychodynamic levels these offenders' actions were not at all "nonsensical." In our article we categorized the following (nonmutually exclusive) psychodynamic motivations of (apparently) nonsensical shoplifting 1) as a reaction to stress, 2) as a regressive, symbolic act, 3) as unconscious retribution, 4) as unconscious manipulation, 5) as conscious manipulation, and 6) as a response to actual or anticipated personally meaningful loss.

Our experience also suggests that the alternate diagnoses of conduct disorder or antisocial personality disorder do not often fit the persons who have committed "nonsensical" acts of shoplifting. These sorts of shoplifters, and others who committed various kinds of theft and whose actions appear (only) at a superficial level to be "nonsensical" (but which are not), we termed "atypical theft offenders." We introduced this term elsewhere (3).

The atypical theft offender conceptualization is increasingly appropriately employed by both clinicians and lawyers in Canada and elsewhere. It is hoped that, with further refinement of this conceptualization, at some point this syndrome will be incorporated into a future edition of DSM.

The atypical theft offender syndrome is outlined in greater detail in a book that I am presently completing. Included in this latest project are detailed means of obtaining clinically relevant and judicially useful assessments as well as ways of providing specialized treatment in such cases.

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WILL CUPCHIK, PH.D., C.PSYCH.
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Dr. Goldman Replies

SIR: I would like to thank Dr. Cupchik for pointing out several important editing errors in my article on kleptomania. Indeed, the article by Dr. Cupchik and Dr. Atcheson states that shoplifting losses have been estimated at 24 billion dollars per year and not 40 billion as I stated. Additionally, in my article, I stated, "Kleptomania may account for a substantial proportion of the staggering 40 billion dollars in business losses each year (1)." While I attributed this to Drs. Cupchik and Atcheson, it is misleading since I meant only to use the statistic. Indeed, my sentence should have read, "Since shoplifting losses have been estimated at 24 billion dollars (1) it is possible that kleptomania may account for some of this loss."

Editing errors aside, I attempted to incorporate cases that approximated *DSM-III-R* criteria but often found that the data were insufficient to accomplish this. In discussing Dr. Cupchik and Atcheson's loss-substitution-by-shoplifting hypothesis in my article and given little data from which to draw diagnostic conclusions, I suggested that some of his patients may have suffered from kleptomania, a notion strongly disputed by Dr. Cupchik based on his interpretation of the *DSM-III-R* criteria.

In actuality, many of the vignettes presented by Drs. Cupchik and Atcheson in their article contained characteristics not inconsistent with the findings of my review of the literature. Indeed, their article revealed examples of those who, for example, had sexual disturbances, anxiety and depression, risk taking, a sense of excitement, remorse and embarrassment, or uncontrollable drives.

Furthermore, in using *DSM-III-R* to rule out kleptomania in his letter, Dr. Cupchik states that his patients used theft, for example, as a means of exercising either conscious or unconscious retribution or manipulation and thus the thefts are not "nonsensical"—of this I have no doubt. Indeed, the majority of early psychoanalytic writers felt that kleptomania was motivated by unconscious revenge or anger against, for example, ambivalently held objects. While *DSM* states that the theft cannot be the result of anger or vengeance, this is taken to mean conscious anger or vengeance. *DSM* does not discuss unconscious motivations when describing impulse disorders, nor should it, as it would make unconscious anger fair game. Dr. Cupchik may be confusing diagnostic criteria with etiology. Indeed, the fact that the acts are not nonsensical from a psychodynamic point of view, as Dr. Cupchik stated, is true but irrelevant as it pertains to diagnostic or inclusion criteria. I am also concerned about Dr. Cupchik's reductionistic model for theft and his suggestion that a new category be created for possible inclusion in *DSM*. Putting people into a myriad of different diagnostic categories based on their varying unconscious motivations seems fine for psychodynamic texts, but not for *DSM*, since the point of this manual is diagnostic and not etiologic. At best, I would perhaps argue for a less restrictive set of diagnostic criteria for kleptomania, rather than creating new disorders.

As for Dr. Cupchik's thesis that the "moral majority" represents a subgroup distinct from those with kleptomania or other stealing behaviors, I suggest that those who do not meet the criteria of the "moral majority" end up in prison, rather than in a psychiatric institute where they can be studied, because they are deemed less interesting or less likely to be rehabilitated by the courts and ostensibly more guilty because of their diminished financial or social status. I suggest that the drive to steal—once, occasionally, on a sustained level, "nonsensically," or otherwise—can be found in members of all socioeconomic groups. The one-time or infrequent offender, however, may give us clues and insights into the more severely ill.

MARCUS J. GOLDMAN, M.D.
Boston, Mass.

Clozapine Concentrations and Clinical Response in Schizophrenic Patients

SIR: Paul J. Perry, Ph.D., and his colleagues (1) have reported a study of 29 inpatients suffering from refractory schizophrenia who received approximately 400 mg/day of clozapine for 4 weeks. The investigators claimed to have identified a mini-

mum therapeutic plasma clozapine concentration of 350 ng/ml. The basis of their conclusion was on a categorization of the patients into "responders" and "nonresponders" and subsequent analysis of true and false categorizations with receiver operator characteristic curves.

The use of receiver operator characteristic curves to depict concentration-response relationships may be justified when the response variable is clearly categorical and binary but presents difficulties when there is a continuous variation in the degree of response which must be arbitrarily dichotomized in order to be accommodated in the receiver operator characteristic model. The accepted method in this area is to employ a correlational analysis of concentration and response, both to be considered as continuous variables. Fortunately, the authors have provided complete data from this study, enabling us to perform such an analysis.

Dr. Perry and colleagues used a definition of response which was derived from a clozapine study by Kane et al. (2): namely that "improvement or response was defined as a 20% or greater change in the total Brief Psychiatric Rating Scale (BPRS) score from baseline to the end of week 4 of fixed dosing and a final BPRS score of 34 or less." We constructed alternative receiver operator characteristic curves, using slightly different definitions of response (20% and 30% improvement over baseline without any minimum score) and found no plasma level that discriminated reliably between "responders" and "nonresponders," suggesting that their finding was a product of the particular definition of response that they employed.

Correlational analysis revealed no significant correlation (r between -0.16 and -0.32) between degree of clinical improvement, defined as either absolute or proportional improvement over baseline, and any measure of plasma drug concentration (clozapine, norclozapine or total, expressed in absolute or logarithmic terms). A further analysis by sex revealed some unexpected findings. Even though the mean values for men and women did not differ on any clinical or drug-related variable, the correlation between response and total clozapine plasma levels was significantly negative for men ($r = -0.51$ for BPRS score improvement, $p < 0.05$; $r = -0.45$ for percent improvement, $p < 0.05$) but positive, although not significantly so, for women ($r = 0.50$ and $r = 0.52$, respectively). Similar results were obtained when clinical improvement was correlated with clozapine or norclozapine levels or the log-transformed values. Furthermore, correlations for clozapine and clozapine plus norclozapine were reliably different for men and women ($p < 0.05$; two-tailed test).

It is unclear whether the plasma levels were obtained at consistent time intervals after the clozapine dose was administered. It is possible that the lack of correlation between therapeutic response and plasma levels and the puzzling results obtained by examining men and women separately may have been a result of variations in the blood sampling time from the last dose.

We remain unconvinced that the reported data support the notion of a therapeutic threshold for clozapine, but we suspect one may be established when lower levels are considered.

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JAMES A. OWEN, PH.D.
NICHOLAS J. DELVA, M.D.
J.S. LAWSON, PH.D.
Kingston, Ont., Canada

Dr. Arndt Replies

SIR: We appreciate the interest Dr. Owen and his colleagues show in our article dealing with response to clozapine. They point out what appears to be a lack of correlation between clinical improvement and plasma drug concentration. As we discussed in response to a previously published letter (1), we did perform a correlational analysis and the results were significant. To recapitulate: a significant multiple correlation of BPRS at week 4 was found with mean weekly clozapine controlling for baseline BPRS. One patient described elsewhere (2) with neuroleptic malignant syndrome was excluded from the analysis.

On the subject of using receiver operator characteristic curves and using correlations, we feel that each approach has its place. An early version of our article did include both types of analysis. In the interest of space and relevance, however, this portion of our results was deleted from the published version. Correlation coefficients determine if, and to what extent, variables are related in a linear fashion and how well the regression equations predict points on one scale. However, correlations offer little direct information regarding decisions about specific patients. For instance, a linear scale only suggests more or less of something and not a presence or absence, response or nonresponse. We dichotomized our linear scale for two reasons. As decisions need to be made about the success of a treatment, we felt that it was more clinically meaningful to analyze response versus nonresponse rather than to assess our ability to predict points on an arbitrary rating scale, the BPRS. We also used the specific dichotomizing criteria to allow for comparison with previous research in this area (3).

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STEPHAN V. ARNDT, PH.D.
Iowa City, Iowa

Identification of Mood Variance in Depression

SIR: Donald P. Hall, Jr., M.D., and colleagues (1) suggested that the self-rated mood of depressed subjects during daytime hours shows greater variability and has ultradian rhythms of greater amplitude than that of normal subjects. Although the authors carefully identified several limitations of their study, two specific aspects of the study warrant further comment.

First, the authors identified an "ultradian rhythm" for each subject using only 12 hourly self-ratings. The crossover

method used by the authors will identify a cycle in almost any data. Whether this cycle has any intrinsic meaning as a characteristic of the individual—or indeed any ultradian rhythmicity—requires repeated measures to determine whether the values calculated for the length and amplitude of the cycle are consistent across days. The complex demodulation analysis illustrated in figure 3 results in "highly accurate" curve fitting because it permits the amplitude of the fitted cycle to vary markedly across time. Therefore, interpreting the analysis as supporting the existence of an ultradian rhythm with a specific amplitude seems to go well beyond the available data.

Second, several characteristics of the depressed patient group raise questions about the meaning and generalizability of the observed higher mood variability. The depressed group was diagnostically heterogeneous (as was the comparison group of staff members and paraphilic patients). The depressed patients were not very depressed—the mean Hamilton Rating Scale for Depression score was only 16 and the mean Visual Analogue Mood Scale score was 41. The medication status of the patients was not specified, and the observed mood variability may in part have reflected a response to antidepressant medications. Finally, axis II diagnoses were not reported.

The mood pattern in the depressed group—mild to moderate depression with higher mood variability than the comparison group—is similar to that which we documented in "depressed" patients with borderline personality disorder using twice daily Visual Analogue Mood Scale ratings over 2 weeks and was quite different from the pattern we observed in medication-free patients with major depressive disorder—moderate to severe depression with little variability (2). The authors' claim that depressed patients in general have greater mood variance than nondepressed individuals should be treated with some skepticism. The varieties of depressive experience are many, and the mechanisms of mood regulation underlying them are likely to be correspondingly varied.

As the authors suggested, deceptively simple tools like the Visual Analogue Mood Scale may well contribute to our understanding of the mechanisms of mood regulation and to better differentiation among patients with "depression," particularly as these tools are applied in larger populations with carefully delineated clinical characteristics, including the presence or absence of comorbid axis II disorders.

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REX WILLIAM COWDRY, M.D.
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Dr. Hall and Associates Reply

SIR: Dr. Cowdry's comments are noted and reflect a thorough review of our study; however, we question the use of his data to criticize our findings. Limitations in the design of his own study may explain the discrepancy in our reports. His methods are based on the assumption that mood varies in a random pattern. Our study, however, suggested that mood variance is not random but follows a cyclical pattern. By using

only two mood assessments (morning and evening) over the course of the day he fails to detect cycles less than 24 hours in length. Our study utilized 13 hourly mood assessments over the course of the day and represents a more valid method of assessing intradaily mood variance.

Further, our finding of increased mood variance in depressed persons is conceptually consistent with research supporting a dysregulation hypothesis of depression. This theory holds that affective disorders may involve a failure in the regulation of neurotransmitter systems rather than simply increasing or decreasing the baseline activity (1). Perturbation of homeostatic mechanisms with the establishment of a new baseline of mood appears to be accompanied by increased variability around that baseline.

Our article represents the first report describing a detailed methodology to approach the study of ultradian cycles of mood. One other study has described ultradian cycles of mood (in normal subjects), but methodology was only briefly described (2). As an exploratory study, our methods and focus will require modification as research continues. Although we disagree with Dr. Cowdry's implication that complex demodulation can be used to demonstrate cycles with a high degree of accuracy ($r^2=0.95$) in almost any data, we agree that the program does not provide the specificity to be used alone as a method to detect cycles. For this reason, we also relied on visual inspection of the raw data time series plots. We readily observed ultradian cycle periodicity in the raw data plots of the majority of subjects tested, as we sought to illustrate in figures 2 and 3 of our article. Complex demodulation is not a required element of this study and in future studies it may be necessary to replace it as a method to describe goodness of fit. Amplitude and period can be calculated without complex demodulation by simple measurements of raw data plots.

Regarding the sample populations utilized in our study, we designed the study to make an exploratory assessment of mood variance in depression. Follow-up studies are required to look at more homogeneous depressed groups and control groups. Dr. Cowdry's criticism of our use of heterogeneous groups appears inconsistent when he has cited the homogeneous groups in his own study as a possible bias because such groups may be atypical for the disease. In the absence of research wards designated for the study of nonmedicated patients, it was not feasible to perform this study on nonmedicated patients, and we hope that investigators with such capability will evaluate this question.

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Twins and Eating Disorders

SIR: Kenneth S. Kendler, M.D., and his associates reported in their excellent article (1) that, in determining zygosity, they found 590 monozygotic twin pairs and 440 dizygotic twin pairs, with three pairs uncertain. Thus 590/1033 or 57.3%

were monozygotic. The usual proportion of monozygotic twins is 33%. This discrepancy suggests a sampling bias in this cohort study of female twins.

Dr. Kendler and colleagues indicated that one limitation of their study was that twins may not be representative of the general population with respect to eating disorders. Given their finding of a high proportion of monozygotic twins in their sample, the findings in this study may not be representative of twins in the general population either. Replication of these points in future studies is indicated to expand our understanding of the epidemiology of eating disorders.

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JONATHAN G. SOLOMON, M.D.
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Dr. Kendler Replies

SIR: I appreciate Dr. Solomon's interest in our recent article. Dr. Solomon is correct that in Caucasian populations of both same-sex and opposite-sex twin pairs approximately one-third of all twins are monozygotic (1). However, in samples of only same-sex pairs, such as those we studied, approximately 50% of the pairs are monozygotic. This is only an approximation, as the rate of twinning (particularly dizygotic twinning) varies across countries, even among Caucasian populations (1). It is likely that we have a slight excess of monozygotic twins in this study, but the excess is far smaller than Dr. Solomon would suggest. For example, in volunteer twin studies where subjects are recruited through advertisements in newspapers, newsletters, etc., approximately two-thirds of the population is monozygotic (2). Thus, our results are consistent with a slightly increased probability that monozygotic female same-sex pairs will cooperate compared to dizygotic pairs. However, this bias is probably a relatively modest one.

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KENNETH S. KENDLER, M.D.
Richmond, Va.

Regarding the Use and Accuracy of the Family History Method

SIR: The title of a recent article by Kenneth S. Kendler, M.D., and colleagues (1), implies that family history obtained from an affected twin reflects her personal psychiatric history rather than the true history of the parent on whom she is reporting. Unfortunately, the design of this study and the data reported do not support this conclusion.

For example, the authors concluded that family history is substantially influenced by the informant's psychiatric history, but that the size of the sample of twin pairs discordant for alcoholism was too small to provide a powerful test. This

is extremely misleading. The absence of an association for alcoholism is not due to insufficient power, but due to the strong agreement between the twins on their parents' diagnosis of alcoholism. From the authors' data, one can calculate kappas of 0.73 and 0.68 for twin agreement on the mother's and father's alcoholism history, respectively. What the authors have demonstrated for alcoholism is evidence that family history is a reliable study method.

The design of the study by Dr. Kendler and colleagues cannot yield information regarding the relative sensitivity or specificity of affected versus unaffected twins in reporting on their parents since we do not know the "true" diagnostic status of the parent. Table 1 showed that even unaffected twins reported ill parents without agreement from the other twin. Yet, the statistical method used by Dr. Kendler and colleagues tested for association between informant diagnosis and parent diagnosis. Thus, it incorrectly treated all cases reported by the affected twin (unconfirmed by the unaffected twin) as false positives and all cases reported by the unaffected twin (unconfirmed) as true cases.

In the absence of data on the parents' "true" diagnosis, we have no reason to believe that one or the other twin was more or less accurate in the history she provided. An affected twin may well have reported an affected parent more frequently, but there is no reason to believe that this constitutes an incorrect or biased report, as implied by the article's title.

An appropriate test of the accuracy of the family history method would compare agreement and disagreement between the twins' family history report and a "gold standard" such as direct interviews with the parents. Such a study would produce estimates of the diagnostic sensitivity and specificity of the family history method. In fact, Thompson et al. (2) used this method and have reported that family history yields high specificity and modest sensitivity for major depression and alcoholism, and low sensitivity for generalized anxiety disorder.

In order to prove that the affected status of the informant introduces systematic diagnostic bias to family history, one would have to show that affected informants overestimate illness (report false positives) and unaffected informants underestimate illness (report false negatives). The authors have not done this. To suggest that the family history method is flawed in the absence of such data is not justified.

Even the most thorough investigator will need to rely on family history information for some relatives because of death or refusal of direct interview. Assertions that such history is biased are premature.

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EWALD HORWATH, M.D., M.SC.
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Dr. Kendler Replies

SIR: While I appreciate Dr. Horwath's interest in our recent article, I disagree with several of his conclusions. He is, however, completely correct in asserting that our design does not allow us to determine the "relative sensitivity or specificity of

affected versus unaffected twins in reporting on their parents." We wrote in the article: "Our results do not address the crucial question of whether individuals with a history of a psychiatric disorder are more or less accurate informants about psychiatric illness in their relatives than are individuals who report no personal psychiatric history." We have, in the last 2 years, personally interviewed most of the living parents of these twins and intend to directly address this issue shortly.

I also agree with Dr. Horwath that our sample size of twins discordant for alcoholism was too small to provide a powerful test of our hypothesis. This small number was due to several factors, especially the low base rates for alcoholism in this sample and the relatively high agreement between twins in their reporting on alcoholism in their parents.

I am unable to follow Dr. Horwath's logic, however, when he claims that we treated all cases reported by an affected twin as false positives and those reported by the unaffected twins as true cases. Our design was entirely agnostic with respect to which twin from discordant pairs was accurate in her family history diagnosis. We merely tested the hypothesis, which was confirmed for major depression and generalized anxiety disorder, that in discordant pairs, affected twins more often reported a family history diagnosis in their parents than did unaffected twins.

Dr. Horwath goes on to claim that we have no basis to conclude from our data that the family history is flawed. Again, I disagree. While he correctly points out that we cannot discriminate between false positive reports from affected individuals and false negative reports from unaffected individuals, our results do clearly suggest that at least one of these factors *must* be operating. Otherwise, we would have found no association between personal psychiatric diagnosis and family history reporting in our discordant pairs. Since either false positive reports from affected individuals or false negative reports from unaffected individuals constitute a bias in the family history method, our conclusions stand.

KENNETH S. KENDLER, M.D.
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Prevalence of Abnormal Movement Disorders Associated With Neuroleptics

SIR: Vikram Khot, M.D., and Richard Jed Wyatt, M.D. (1), deserve our thanks for their review of published data on the prevalence of tardive dyskinesia and of spontaneous dyskinesia in different age groups. When considering the alleged prevalence of the former, it is clearly essential to subtract the latter to arrive at a true prevalence figure for "real" tardive dyskinesia. However, I am unhappy about one aspect of their study. They accepted in their group of "spontaneous" dyskinesias any patient with a rating of 2 or higher for whom the authors "provided reasonable assurance that the patient did not have a history of neuroleptic exposure of more than 3 months." This was on the basis of the assumption that neuroleptic-associated dyskinesia does not begin in patients who have been treated with neuroleptics for less than 3 months. However, this argument is potentially circular. What we really need to know is the dyskinesia rate in patients who have *never* been treated with neuroleptics. This could then be compared with the rate in a) patients ever treated, b) patients treated for less than 3 months, and c) patients treated for more than 3 months. Are such data available from the studies examined by the authors? and if so, Could they not be presented?

A second, and equally important, question is the prevalence

of permanent tardive dyskinesia in patients withdrawn from neuroleptics. This involves a similar analysis that additionally takes account of the remission rate of tardive dyskinesia at varying time intervals after stopping neuroleptic treatment. Here, the equivalent question is: by how much does the prevalence, at a given number of years after stopping treatment, of neuroleptic-associated dyskinesia exceed that of spontaneous dyskinesia? If one undertook the same exercise, might the two prevalence rates be the same after, say, 5 years? Such an analysis would be of great clinical and medicolegal importance.

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N.P. QUINN, M.D.
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Dr. Wyatt and Dr. Khot Reply

SIR: Dr. Quinn raises an important issue when he asks about the prevalence of abnormal involuntary movements in patients never treated with neuroleptics versus those treated for less than 3 months. While there are probably too few well-controlled studies to reliably assess the incidence across multiple age groups, we believe there is sufficient evidence to conclude that it is rare for tardive dyskinesia to develop within 3 months of treatment. The evidence includes the following observations: 1) In most animal studies, tardive dyskinesia-like movements are not observed until at least 2-4 months after neuroleptics are initiated (1). 2) Only a few human studies report the occurrence of tardive dyskinesia within three months of introducing a neuroleptic, and some of these reports may include patients with initial dyskinesias (initial dyskinesia quickly and spontaneously remits and therefore is different than tardive dyskinesia). If tardive dyskinesia were more common during this period, one would expect to see a flood of case reports. 3) Prospective longitudinal studies of tardive dyskinesia development indicate about a 3% incidence in the first year of treatment for most age groups (2) (elderly patients may be at greater risk [3]). If this occurrence is evenly distributed throughout the first year, the incidence for the first 3 months would be less than 1%. 4) Of several hundreds of tardive dyskinesia patients we have seen, only one has developed tardive dyskinesia-like movements early in the course of neuroleptic administration. In this case, a 66-year-old woman developed mouth and tongue movements 3 months after beginning treatment for an acute psychotic episode related to a small stroke. For these reasons we believe it is unlikely that including patients with less than 3 months neuroleptic exposure in our never-treated group significantly distorted the prevalence of spontaneous dyskinesia.

Dr. Quinn also raises the interesting question of whether neuroleptic-induced abnormal movements dissipate when treatment is discontinued to the point that their incidence approaches that of spontaneous dyskinesia. While there are no published studies that clearly answer this question, this incidence can be estimated by making several assumptions. Casey (4), while following a group of 27 middle-aged tardive dyskinesia patients (although patients were on neuroleptics, it is not clear that some of them did not have spontaneous dyskinesias) for 5 years, attempted to gradually reduce the neuroleptic dose and ultimately to discontinue it. Discontinuation was possible in 10 patients. Of these 10, the Abnormal Involuntary Movement Scale score

for eight decreased by more than 50%; of the eight patients, those who showed abnormal movements at the end of 5 years were still improving. Assuming the 10 patients in the Casey study are representative of the 50- to 59-year-old tardive dyskinesia patient population (who can tolerate neuroleptic discontinuation), we would predict that 20% of tardive dyskinesia patients will have permanent abnormal involuntary movements (as defined by less than a 50% decrease after 5 years following neuroleptic discontinuation). In figure 2 of our report, we noted that about 15% of patients, ages 50-59, treated with neuroleptics for more than 3 months will develop "true" tardive dyskinesia. Thus, 3% (20% of 15%) of all 50- to 59-year-old patients exposed to neuroleptics would be expected to develop permanent tardive dyskinesia. Paradoxically, the risk of spontaneous dyskinesia for patients in this age group is 25%, or more than 8 times greater than the risk for permanent tardive dyskinesia.

The Casey study is substantially different than a study by DeVeaugh-Geiss (5), which reported little or no further improvement in tardive dyskinesia patients 1 year after neuroleptic discontinuation. It is, however, in agreement with a study by Klawans et al. (6) as well as an early review of discontinuation studies in the literature, which concluded that the point prevalence of persistent tardive dyskinesia (8%) was not much different than that of spontaneous dyskinesia (5%).

Despite our attempts to estimate incidences of tardive and spontaneous dyskinesias, there are many questions, including those raised by Dr. Quinn, that require further inquiry.

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RICHARD JED WYATT, M.D.
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Involuntary Facial Movements, Not All Medication-Induced

SIR: An area of the article by Joanne D. Wojcik, R.N., M.S., C.S., and associates (1) that ought to raise concern is their report that of the 32 patients with tardive dystonia, at last evaluation as many as 18 had only facial movements (10 patients with blepharospasm and 14, grimacing). Such movements are commonplace and usually idiopathic (2, 3). Physicians should not automatically accept all involuntary facial movements as having been induced by medications, especially in this series where the medications were diverse in structure, and their administration preceded the development of the movements by more than 6 years in 11% of cases.

Moreover, whatever the cause, blepharospasm, more gen-

eralized involuntary facial movements (Meige's syndrome), hemifacial spasm, and spasmodic torticollis and related involuntary neck movements may now be treated with intramuscular injections of botulinum toxin (4). This novel therapy, although sometimes complicated by temporary muscle weakness and need for repeated injections about every 3 months, markedly reduces the involuntary movements without exposure to systemic side effects of previously reported medications, including tetrabenazine, clonazepam, bromocriptine, and anticholinergics, which have generally been ineffective. Botulinum toxin injections also hold promise for treatment of the classic, buccolingual form of tardive dyskinesia.

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Dr. Cole and Associates Reply

SIR: We appreciate Dr. Kaufman's thoughtful reading of our paper, but do not concur with all his conclusions. In the absence of any basis for determining when blepharospasm is or is not idiopathic, its occurrence with other signs of dyskinesia in patients taking neuroleptics should be considered tardive dystonia.

The time from first neuroleptic treatment to onset of abnormal movements in our sample (over 6 years) is not at all unusual in nondystonic tardive dyskinesia and would therefore not make Meige's syndrome any more likely. Dr. Kaufman assumes that "diversity in structure" of the antipsychotics taken by our patients argues against their having the same disorder. So far, all dopamine blocking drugs, irrespective of structure, have been found to be associated with tardive dyskinesia. The common pharmacology seems more relevant than the actual chemical structure.

Botulinum toxin injections have provided marked benefit for patients with severe persistent dystonia of any etiology. However, its efficacy in lingual dystonia has been limited by dysphagia in nearly half the patients treated (1). Many patients with presumed tardive dystonia require maintenance antipsychotic treatment, and clozapine may help both the psychosis and the dystonia. To our knowledge, clozapine has not been tried in Meige's syndrome.

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Antiglucocorticoid Effects of DHEA-S in Alzheimer's Disease

SIR: In an article by Owen M. Wolkowitz, M.D., and associates (1) the possibility of specific corticosteroid-related cognitive impairments is stressed. These authors speculate that anticorticoid hormonal treatment could ameliorate cognitive impairments associated with endogenous hypercortisolemia. Chronic glucocorticoid administration leads to hippocampal damage in the rat and, due to a dysfunction of the hypothalamic-pituitary-adrenal axis, to progressive dementia (2). Sunderland et al. (3) demonstrated reduced plasma concentrations of dehydroepiandrosterone-sulfate (DHEA-S) in Alzheimer's disease and discussed the possible importance of this hormone in the central nervous system. DHEA-S was shown to block enzymatic effects of glucocorticoids (4), thus, a certain part in the progression of Alzheimer's disease may be caused by the decrease of DHEA-S and its antiglucocorticoid functions.

In our own series, 24 drug-free patients with Alzheimer's disease (11 women, aged 58-86; 13 men, aged 62-88) and 50 normal control subjects (23 women, aged 18-81; 27 men, aged 21-81) were studied. Blood samples for DHEA-S (ng/ml) and cortisol (μ g/dl) plasma measurements were obtained after an overnight fast, stored at -20°C , and tested in the same assay by radioimmunoassay. The DHEA-S/cortisol ratio was calculated in all subjects studied. Data were analyzed by Wilcoxon's test. Diagnosis of Alzheimer's disease was established by DSM-III-R and confirmed by X-ray CT, excluding patients with multi-infarct dementia, and single photon emission computed tomography, tracing the parietotemporal hypoperfusion typical for Alzheimer's disease (5, 6). In patients with Alzheimer's disease, routine laboratory tests, vitamin B₁₂, folic acid, and T₃, T₄, and thyrotropin serum levels were within normal limits.

A strong negative correlation was found between age and DHEA-S ($r=-0.8$ for women and $r=-0.7$ for men) (4, 5), but no significant correlation was found between cortisol levels and age, therefore, the DHEA-S/cortisol ratio dropped remarkably in older normal subjects (older than 60 years old) as compared to young individuals (45 years of age or younger) ($p<0.01$). Interestingly, a trend was found for a lower DHEA-S/cortisol ratio in Alzheimer's disease patients compared to age- and sex-matched control subjects ($p<0.1$), indicating that this ratio could be an appropriate measure for the effects of DHEA-S as an antiglucocorticoid by which subjects at risk for the neurotoxic effects of glucocorticoids could be identified (6). These previous results suggest a possible relation of cognitive impairment to circulating corticoid levels, as mentioned by Dr. Wolkowitz and colleagues (1), and they indicate a possible role of DHEA-S in diminishing cortisol effects on hippocampal cells avoiding progressive hippocampal degeneration in Alzheimer's disease (6).

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Dr. Wolkowitz and Associates Reply

SIR: We have previously reported that increased circulating corticosteroid levels may be associated with cognitive impairment in certain conditions. Dr. Friedrich Leblhuber, M.D., and colleagues suggest that levels of other steroid hormones such as dehydroepiandrosterone (DHEA) and DHEA-S may also be relevant in determining cognitive performance since such hormones may have "antiglucocorticoid" effects. We agree with their suggestion that examination of cortisol/DHEA-S ratios may be more informative than examination of levels of either hormone individually.

While the nature of possible antiglucocorticoid effects is unknown, several authors have reported physiological antagonism by DHEA of corticosteroid effects such as thymic involution and suppression of lymphocyte proliferation (1-4). We propose that, in addition to such "pharmacodynamic" effects, DHEA may have a "pharmacokinetic" effect on circulating cortisol levels. We have begun a preliminary, open-label study examining the possible antidepressant and cognition-enhancing effects of orally administered DHEA, 30-90 mg/day, in patients with major depressive illness who have low baseline DHEA or DHEA-S levels. One interesting preliminary finding to emerge from this study is that pharmacologically induced increases in DHEA levels (resulting in normalized age-corrected levels) are significantly correlated with decreases in 4:00 p.m. serum cortisol levels ($r = -0.78$, $df = 5$, $p < 0.04$). This finding, if replicated in larger-scale studies, would indicate that DHEA may indeed have "antiglucocorticoid" effects, perhaps through a "pharmacokinetic" action. Prior studies have suggested that DHEA sulfuric ester may decrease pituitary ACTH release in rats (4), and that DHEA may inhibit various enzymatic activities (5) also resulting in decreased cortisol biosynthesis. These findings raise the possibility that DHEA administration may have salutary effects in ameliorating corticosteroid-associated behavioral and cognitive impairment in certain patients.

An additional approach, involving the administration of precursor steroid hormones, has also been recently proposed. The biosynthesis of steroid hormones begins with cholesterol, from which the glucocorticoids, mineralocorticoids, and sex steroids all derive. Pregnenolone, a key cholesterol metabolite, is the major precursor for the steroid hormones. Its formation, regulated by pituitary hormones, may become rate-limiting in aging, stress, and other conditions, resulting in steroid imbalances. The recent findings of a striking memory-enhancing effect of pregnenolone and literature showing virtually no human toxicity, suggest that administration of pregnenolone

may help reestablish normal relations among the various steroids when abnormalities occur. We are proceeding with investigations to test these hypotheses in patients with depression and Alzheimer's disease.

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Credibility of Patients in Psychiatric Research

SIR: I must agree with the criticism by F. Wayne Furlong, M.D. (1), that the methods used by Barbara Sanders, Ph.D., and Marina H. Giolas, M.D. (2, 3), and, in particular, by George R. Brown, M.D., and Bradley Anderson, M.D. (4, 5), may have resulted in false or exaggerated reports of childhood abuse. Although the latter two authors replied that they exercised great care to guard against this, the very nature of their paradigm suggests otherwise. The interviewers directly asked psychiatric patients about abusive experiences and would repeat these questions if an affirmative response was not at first obtained. The potential for demand characteristics with such explicit questioning procedures is obvious and would be a problem even with normal subjects.

I would also like to comment on the reply by Dr. Sanders (2) that "for any verbal report measure, what we know depends on how willing we are to believe our subjects." I fail to see how holding private reservations about the accuracy of an abuse memory necessarily implies "discrediting the witness." I also fail to see how believing all such memories to be accurate is somehow a "more parsimonious" approach, especially when belief in some memories requires acceptance of such nonparsimonious constructs as repression and dissociation. Finally, I take issue with Dr. Sanders' statement that high dissociating subjects, because they have greater pain tolerance, would therefore tend to minimize rather than exaggerate reports of abuse. One could just as easily argue that their ability to tolerate aversive stimulation enables them to uncover (or confabulate) more severe memories of abuse. The problem here is that one can always find some piece of evidence that can be twisted to defend virtually any position. Such loose conceptualizing will do little to advance our understanding of the issue.

Contrary to Dr. Sanders' opinion, what we know depends

not on belief but rather on our willingness to critically challenge our assumptions and to entertain alternative explanations. For example, DeGree and Snyder (6) have shown that subjects placed in ego-threatening situations are then more likely to report traumatic life events. They interpret these results as possibly indicating an attempt by subjects to provide justification for potential failure. Could a similar effect play a role in altering abuse memories reported by psychiatric patients? Such a line of investigation might prove more fruitful than further correlational studies based upon largely unsubstantiated, and essentially nonfalsifiable, self-reports.

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Dr. Sanders Replies

SIR: The issue Dr. Powell addresses is an important one, and I welcome the opportunity his comments afford to expand my reply to Dr. Furlong. For clarity, I will restrict my remarks to questions concerning my own paper and will not comment on the work of Drs. Brown and Anderson.

What is to be explained in our research is the significant correlation in disturbed adolescents between the degree of dissociation and the degree of recalled childhood stress or trauma. The relationship was positive, that is, higher dissociators reported higher levels of childhood stress. This correlation cannot be dismissed simply by proposing that high dissociators are "unreliable" in reporting or remembering their childhoods, since mere unreliability, with some subjects overestimating and others underestimating the degree of trauma they had experienced, would not produce a relationship between dissociation and childhood experience.

To account for the correlation as an artifact of memory or reporting, one must propose that high dissociators, as a group, are biased in reporting or remembering the past. More specifically, since the correlation was a positive one, one must propose that high dissociators *overestimate* the stressfulness of their childhoods, as Dr. Powell suggests they might. I agree with Dr. Powell that such a position could be defended, given our present state of knowledge; however, as he indicates, in my earlier remarks I presented some evidence for the opposite bias, i.e., that high dissociators might *underestimate* the degree of trauma they had experienced. This bit of data on the other side of the argument simply indicates our inability to resolve this issue on the basis of existing empirical evidence.

When it comes to speculation concerning the direction of any hypothesized bias, I heartily agree that we can "defend virtually any position."

An important alternative is that dissociation level is linked to any particular childhood reporting bias, but that high dissociators have indeed experienced more traumatic childhoods than low dissociators. This is the alternative I called "parsimonious." I regard it as parsimonious because it fits with a variety of types of evidence suggesting that trauma produces dissociation. We know, for example, that acute trauma may precipitate dissociative experiences, and also that individuals suffering from dissociative disorders very frequently report extremely traumatic episodes earlier in life or in childhood.

In suggesting that we not "discredit the witness," I am asking that we investigate the reliability of these reports rather than simply dismiss them. My argument is that we should not prejudge the issue by assuming that our subjects' memories are distorted or biased. I do not, of course, advocate the uncritical acceptance of self-reports, rather I warn against their uncritical rejection. What is needed is not more speculation, but more study.

BARBARA SANDERS, PH.D.
Storrs, Conn.

Recovery and Shorter Duration of Hospitalization

SIR: In reading the recent article by Gabor I. Keitner, M.D., and associates (1), I wondered why the authors did not consider that two of the five factors most strongly associated with recovery might be related to each other. I am referring to the shorter duration of hospitalization and the absence of more than two previous episodes of hospitalization in the recovered subset of patients. One possible explanation for the finding that less time in hospitals is associated with recovery is that hospitalization itself may contribute to the pattern of morbidity.

Both community psychiatry and its predecessor, military psychiatry, have emphasized the wisdom of treating the patient within his or her life context as close to the scene of trauma as possible and for as brief a time as is necessary for stabilization. In my experience in the military during the Vietnam war, I was taught that the likelihood of rapid recovery diminished considerably when the patient was hospitalized and/or evacuated. Although there is need for hospitalization in some patients with major depression, HMOs and other managed care systems, with their emphasis on outpatient alternatives, have taught us that it is often possible to avoid this major step without compromising care. This article suggests it may be preferable.

It may be speculated that it is not the pattern of recurrent depression or its severity alone that determine morbidity, that the manner and intensity of treatment may be a major determining factor as well. Since neither the recovered nor unrecovered patients were treated with ambulatory alternatives or even particularly brief hospitalization, it would be important to compare these options with traditional, 2- to 3-week inpatient stays. It may very well be that hospitalization, when necessary, involves a kind of "therapeutic window," and that more concerted efforts should be made to avoid it when possible, and to keep it brief when it is unavoidable. If validated, this hypothesis would bring synergy to our sometimes divergent concerns with cost and quality of care.

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MICHAEL J. BENNETT, M.D.
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Dr. Keitner and Associates Reply

SIR: The hypothesis advanced in Dr. Bennett's letter, namely, that hospitalization itself may contribute to morbidity in affective disorder, may be important to test. Our study, however, does not in any way address this issue. More specifically, we do not have data to suggest that avoiding hospitalization is necessarily "preferable."

We noted in our article that "correlation between length of hospital stay and the other variables in the model were neither substantial nor significant." Nonetheless, the technique of log

linear analysis takes into account correlations between variables entered into the model.

We would be cautious about drawing an analogy between the treatment of the sequelae of acute traumatic experiences as in war and the treatment of major depression which may have no relationship to preceding traumatic events. It should also be noted that most of our patients were, in fact, treated unsuccessfully with "ambulatory alternatives."

Although it may well be true that a "therapeutic window" for a successful hospital stay exists, we do not yet know what that window is. At the least, we suspect that this window is likely to be different for different patients depending on the nature of their depressive illness, comorbidity, psychological make-up, and social resources. Although overly prolonged hospitalization may lead to potential problems, so may unduly short hospitalizations.

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Reprints of letters to the Editor are not available.

Corrections

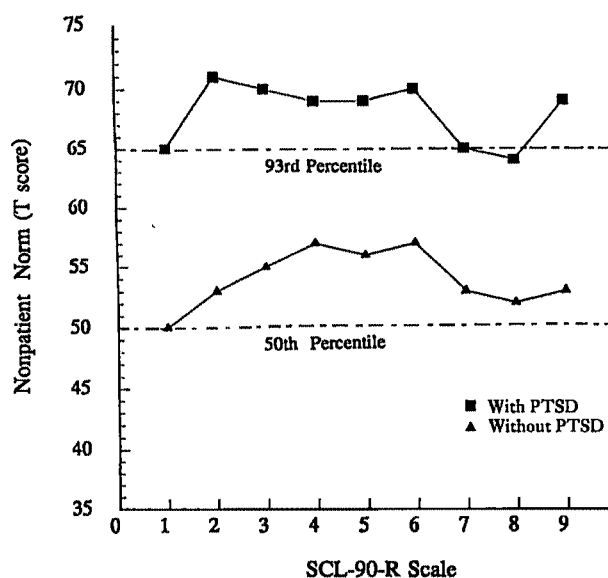
In the article "An Empirical Evaluation of the Global Deterioration Scale for Staging Alzheimer's Disease" by Carl Eisdorfer, Ph.D., M.D., et al. (February 1992, pp. 190-194), on p. 192, second paragraph, seventh line, the words "dependent variables" should be substituted for "independent variables."

The authors of the letter "Clozapine-Induced Priapism" (Joseph Ziegler, M.D., and David Behar, M.D., February 1992, pp. 272-273) thank Dr. Richard Balon for correcting the references. Reference 2 should read "Balon R, Berchou R, Han H: Priapism associated with thiothixene, chlorpromazine, and thioridazine (letter). J Clin Psychiatry 1987; 48:216." In reference 3 also, the journal is J Clin Psychiatry.

In the article "Alprazolam as a Neuroleptic Adjunct in the Emergency Treatment of Schizophrenia" by James G. Barbee, M.D., et al. (April 1992, pp. 506-510), the unit of measurement for alprazolam and haloperidol blood levels described in the fifth paragraph of the second column on p. 508 should be "ng/ml."

In the article "Symptom Responses of Female Vietnam Veterans to Operation Desert Storm" by Jessica Wolfe, Ph.D., et al. (May 1992, pp. 676-679), on p. 678 the key to figure 1 is inverted. The corrected figure follows.

FIGURE 1. Mean SCL-90-R Scores During Operation Desert Storm for Female Vietnam Veterans Grouped by Scores on the Mississippi Scale for Combat-Related Posttraumatic Stress Disorder



1991-1992 Annual Report of the American Board of Psychiatry and Neurology, Inc.

COMPOSITION OF THE BOARD

At its business meeting in July 1991, the American Board of Psychiatry and Neurology (ABPN) elected the following officers, who began their terms on Jan. 1, 1992: Dr. Gary J. Tucker, President; Dr. Stuart A. Schneck, Vice-President; Dr. James H. Shore, Secretary; Dr. Ludwig Gutmann, Treasurer; and Dr. Lenore C. Terr, Executive Committee Member-at-Large.

Dr. Sheldon Miller (psychiatrist, Chicago), nominated by the American Medical Association, was elected to a 4-year term on the board to succeed Dr. Maurice J. Martin, who completed his second 4-year term on Dec. 31, 1991. Dr. Darryl C. De Vivo (neurologist, New York), nominated by the American Neurological Association, was elected to a 4-year term on the board to succeed Dr. William E. Bell, who completed his second 4-year term on Dec. 31, 1991. Dr. Lenore C. Terr (psychiatrist, San Francisco) was renominated and reelected to serve a second 4-year term as a director. Dr. Michael P. McQuillen (neurologist, Lexington, Ky.) was renominated for a second term of 4 years after completing a first term of 1 year. The names of the 1992 ABPN directors follow; those serving second 4-year terms are not eligible for reelection.

From the American Medical Association—psychiatry directors: Dr. Kenneth Z. Altshuler (first term expires Dec. 31, 1992), Dr. Sheldon I. Miller (first term expires Dec. 31, 1995), and Dr. Peter M. Silberfarb (first term expires Dec. 31, 1994).

From the American Psychiatric Association—psychiatry directors: Dr. William T. McKinney (first term expires Dec. 31, 1994), Dr. James H. Shore (second term expires Dec. 31, 1994), Dr. Peter E. Tanguay (first term expires Dec. 31, 1993), Dr. Lenore C. Terr (second term expires Dec. 31, 1995), and Dr. Gary J. Tucker (second term expires Dec. 31, 1992).

From the American Neurological Association—neurology directors: Dr. Darryl C. De Vivo (first term expires Dec. 31, 1995), Dr. J. Donald Easton (second term expires Dec. 31, 1992), Dr. Ludwig Gutmann (second term expires Dec. 31, 1994), and Dr. Stuart A. Schneck (second term expires Dec. 31, 1993).

From the American Academy of Neurology—neurology directors: Dr. Mark L. Dyken (first term expires Dec. 31, 1992), Dr. Marvin A. Fishman (first term expires Dec. 31, 1993), Dr. Michael P. McQuillen (second term expires Dec. 31, 1995), and Dr. Burton A. Sandok (first term expires Dec. 31, 1994).

Dr. Stephen C. Scheiber is the Executive Vice President of the ABPN.

EXAMINATIONS

Part I

At the part I (written) examination on March 31, 1992, 2,974 psychiatrists were examined; 1,788 (60%) passed and 1,186 (40%) failed. A total of 775 neurologists were examined; 431 (56%) passed and 344 (44%) failed. A total of 113 child neurologists were examined; 60 (53%) passed and 53 (47%) failed. Table 1 contains the

numbers of candidates in each year from 1987 to 1992. The next part I examination will be held on March 30, 1993. Applications for that examination are due no later than Sept. 1, 1992, and are available from the American Board of Psychiatry and Neurology, Inc., 500 Lake Cook Rd., Suite 335, Deerfield, IL 60015.

Added Qualifications in Geriatric Psychiatry

At the second geriatric psychiatry (written) examination, on March 31, 1992, 578 geriatric psychiatrists were examined; 359 (62%) passed and 219 (38%) failed. There will not be a geriatric psychiatry examination in 1993. It is anticipated that the next geriatric psychiatry examination will be held in 1994.

Added Qualifications in Clinical Neurophysiology

At the first clinical neurophysiology (written) examination, on March 31, 1992, 278 clinical neurophysiologists were examined; 227 (82%) passed and 51 (18%) failed. Of those totals, four who passed and one who failed have primary certification in psychiatry; the remaining individuals have primary certification in neurology or neurology with special qualification in child neurology. There will not be a clinical neurophysiology examination in 1993. It is anticipated that the next clinical neurophysiology examination will be held in 1994.

Added Qualifications in Addiction Psychiatry

The first examination for added qualifications in addiction psychiatry will be held in concert with the next part I examination, to be held on March 30, 1993. Applications for that examination are due no later than Sept. 1, 1992, and are available from the American Board of Psychiatry and Neurology, Inc., 500 Lake Cook Rd., Suite 335, Deerfield, IL 60015. It will be held at the same sites as the part I examination and will be approximately 3½ hours long. This will be a multiple-choice written examination. The ABPN anticipates administering this examination on average once every 2 years.

Part II

At the 1991 part II (oral) examinations held in Los Angeles (Jan. 13-15), New Orleans (April 14-16), and Philadelphia (Oct. 27-29), 1,881 psychiatrists, 420 neurologists, and 72 child neurologists were examined. For statistics on these examinations, refer to table 2. The examination sites for 1992 are Atlanta (Jan. 10-12), San Antonio, Tex. (April 5-7), San Francisco (June 14-16), and New York (Nov. 15-17).

The current fees for examination are as follows: application fee=\$300, part I examination fee (submitted with the application fee)=\$300, part I reexamination fee=\$300, part II examination fee=\$600, part II reexamination fee (for psychiatry candidates, failure of major; for neurology candidates, failure of major or failure of major and minor)=\$600, part II reexamination fee (for neurology candi-

TABLE 1. Candidates for ABPN Part I (Written) Examination, 1987–1992

Physician Status	Number of Candidates					
	1987	1988	1989	1990 ^a	1991	1992
Met requirements	2,649	2,861	3,134	3,189	3,642	4,382
Accepted examination	2,477	2,782	3,092	3,169	3,604	4,345
Took examination	2,255	2,471	2,725	2,829	3,211	3,862

^aStatistics on 1990 examination in previous annual reports were incorrect.

dates, failure of minor)=\$400, added qualifications application fee=\$300, added qualifications examination fee (submitted with the application fee)=\$500, added qualifications reexamination fee=\$500.

BOARD DECISIONS AND ITEMS OF INTEREST

1. The American Board of Medical Specialties approved the application of the ABPN for certification for added qualifications in addiction psychiatry at its September 1991 meeting. The Committee on Certification for Added Qualifications in Addiction Psychiatry was appointed in October 1991 and held its first meeting in December 1991. For 1992 the committee membership includes Dr. Sheldon Miller, Chair (ABPN psychiatry director, Chicago); Dr. Marc Galanter, Vice-Chair (New York); Dr. Richard Frances (Newark, N.J.); Dr. Edward Kaufman (Orange, Calif.); Dr. Edward Khantzian (Haverhill, Mass.); Dr. Thomas Kosten (New Haven, Conn.); Dr. Collins Lewis (St. Louis); Dr. Edgar Nace (Dallas); Dr. George Woody (Philadelphia); and Dr. Roger Walker (Seattle).

The general requirements for added qualifications in addiction psychiatry are as follows. The candidate must be certified by the ABPN in psychiatry. All licensing and training requirements must be met before the application for examination is submitted. A formal application on the original form must be completed and filed with supporting documentation and fees by the deadline; a photocopy of the application will not be accepted. A certificate will be issued for a 10-year time-limited period, after which recertification will be necessary to maintain active certification. The training requirements are as follows. The applicant must have completed a 1-year fellowship in addiction psychiatry in a program approved by the Accreditation Council for Graduate Medical Education (ACGME), beginning no sooner than postgraduate year 5. For the first 5 years admission to examination may be achieved by completing a 1-year fellowship in an addiction psychiatry program that is clearly identified as a U.S. or Canadian program. For the first 5 years admission to examination may also be achieved by spending 25% of practice time treating addiction psychiatry patients. The 1 year of specialized training in addiction psychiatry may be completed on a part-time basis provided it is not less than half-time and is taken at one center.

2. During its July 1991 meeting the ABPN held a conference focusing on recertification. Speakers from other boards of the American Board of Medical Specialties participated and provided useful information. The psychiatry and neurology directors of the ABPN agree that the recertification examinations will be cognitive examinations. It was reaffirmed that the recertification examination given by the ABPN will not be offered to any individual who has not been certified by the ABPN.

A meeting to discuss recertification in psychiatry was held in April 1992. The participants were the ABPN psychiatry directors and representatives from the American Psychiatric Association (APA), the American Academy of Child and Adolescent Psychiatry, the ABPN Committee on Certification in Child and Adolescent Psychiatry, the ABPN Committee on Certification for Added Qualifications in Geriatric Psychiatry, and the ABPN Committee on Certification for Added Qualifications in Addiction Psychiatry. The meeting focused on education and the examination process and format.

3. The ABPN reaffirmed its policy whereby all licensing and training requirements must be met before application for examination. An

TABLE 2. Performance of Physicians Who Took ABPN Part II (Oral) Examination in 1991

Candidate Group	N	Passed and Were Certified		Failed	
		N	%	N	%
All specialties	2,373	1,499	63	874	37
New candidates	1,661	1,140	69	521	31
Reexaminees	712	359	50	353	50
Psychiatry	1,881	1,130	60	751	40
New candidates	1,309	876	67	433	33
Reexaminees	572	254	44	318	56
Neurology	420	317	75	103	25
New candidates	299	228	76	71	24
Reexaminees	121	89	74	32	26
Child neurology	72	52	72	20	28
New candidates	53	36	68	17	32
Reexaminees	19	16	84	3	16

exception is made for residents who complete training after Sept. 1 but before Oct. 1.

4. The ABPN determined that in 1994 there will be two part I (written) examinations, one in March or April and one in October. Effective in 1995 the ABPN will begin administering the part I examination in October instead of in the spring. This is being done in an effort to accommodate residents who wish to take the ABPN certification examinations closer to completion of residency training. The deadline for submitting applications for the spring 1994 examination will be Sept. 1, 1993, and the tentative deadline for applications for the October 1994 examination is Feb. 1, 1994. To be certain of the actual deadline date, individuals should contact the ABPN office and look for announcements in medical journals.

5. The ABPN reaffirmed its policy that every applicant must have an *unlimited* license to practice medicine in a state, commonwealth, territory, or possession of the United States or a province of Canada. At the time of application every applicant is required to submit copies of a current license registration with the expiration date noted, in addition to documentation of all training, photographs, and fees.

6. The documentation of completion of training must specify the exact dates of training. If the documentation is in the form of a letter, the letter must be signed by the training director or chairperson of the program.

7. The ABPN adopted a policy allowing individuals to have more than one application on file simultaneously. It is the applicant's responsibility to contact the ABPN office to avoid possible conflicts in examination scheduling.

8. The ABPN adopted the following policy regarding leave or vacation time during residency training. Leave or vacation time may not be used to reduce the total amount of required residency training or to make up deficiencies in training. The ABPN does not have a policy regarding the amount of leave or vacation time allowed, as each program may develop individual leave or vacation time for the resident in accordance with the overall institutional policy.

9. The ABPN voted that for individuals entering residency training as of July 1, 1994, who are seeking certification in neurology, an acceptable alternative to a full year of internal medicine is a full year in which a minimum of 6 months of training is in internal medicine, and these 6 months cannot include rotations in neurology or emergency medicine. At least 2 of the additional 6 months must be spent in pediatrics and/or emergency medicine. No more than 2 of the remaining 4 months may be spent in neurology.

10. The ABPN voted that for individuals seeking certification in neurology with special qualification in child neurology who are already certified in neurology, no more than 3 months of child neurology training from an adult residency can be credited toward the 12-month additional child neurology requirement during training in an ACGME-approved child neurology residency training program. Nine additional months of child neurology residency training would be needed in a program approved by the ACGME or the Royal College of Physicians (Canada) [RCP(CN)]. In addition, 1 year of general pe-

TABLE 3. Number and Performance of Physicians Who Took Child and Adolescent Psychiatry Examination in 1991

Variable	N	%
Composition of candidates		
Total	342	100
New candidates	272	80
Reexaminees	70	20
Performance		
All candidates	342	100
Pass	205	60
Condition	60	18
Fail	42	12
Fail, must reapply	35	10
New candidates	272	100
Pass	170	63
Condition	60	22
Fail	42	15
Reexaminees	70	100
Pass	35	50
Fail, must reapply	35	50

diatric training in an ACGME- or RCP(CN)-approved program is required.

11. The ABPN voted that individuals seeking certification in neurology with special qualification in child neurology who enter training as of July 1, 1992, may complete the following training for 2 of the 5 years of training: 1 year of training in general pediatrics and 1 year of research in the basic neurosciences. The basic neuroscience pathway was created as an alternative track for residents who are planning a research career in academic child neurology. The year of basic neurosciences would provide training in a research discipline related to child neurology and is intended to increase the trainee's knowledge and ability to compete for federal and nonfederal grant support. The trainee must spend at least 80% of his or her time in basic neurosciences during this year of training. For the purpose of this training track, "basic neurosciences" is defined as laboratory research related to the cellular or molecular basis of neurological diseases. Examples of relevant basic disciplines include molecular neurogenetics, neurochemistry, neuropharmacology, neurophysiology, neuroanatomy, neuroimmunology, developmental neurobiology, biophysics, and cell biology. This track of training must be approved before completion of the total 5 years of training.

12. The ABPN will be reviewing information at its July 1992 meeting in consideration of whether the experimental pediatrics-psychiatry joint training program should become a permanent training track.

13. The ABPN voted to proceed with consideration of offering an examination for certification in forensic psychiatry. A letter of intent and application have been sent to the American Board of Medical Specialties. This should be reviewed and approved no earlier than September 1992, and the earliest time an examination could be administered would be in 1994.

14. The ABPN and the American Board of Physical Medicine and Rehabilitation have established guidelines for combined residency training in neurology and physical medicine/rehabilitation. The guidelines are available from the ABPN office.

15. The ABPN and the American Board of Internal Medicine have established guidelines for combined residency training in neurology and internal medicine. The guidelines are available from the ABPN office.

16. The ABPN and the American Board of Internal Medicine have established guidelines for combined residency training in psychiatry and internal medicine. The guidelines are available from the ABPN office.

17. In conjunction with its summer 1992 policy meeting, the ABPN will be holding a retreat that will consist of two debates focusing on subspecialization and the oral examination.

18. At the 1991 APA annual meeting, the ABPN offered a work-

shop on subspecialization. The ABPN psychiatry directors presented information and responded to questions. In addition, the ABPN Executive Vice President and psychiatry directors continue to participate in plenary sessions and other workshops of APA and the American Association of Directors of Psychiatric Residency Training in an attempt to clarify information and to publicize current issues of interest. A workshop was held at the 1992 APA annual meeting focusing on recertification.

19. At the fall 1991 meeting of the American Neurological Association and the spring 1992 meeting of the American Academy of Neurology, ABPN neurology directors and the Executive Vice President met with the Association of University Professors of Neurology to discuss current issues of the ABPN and to respond to questions. These meetings prove valuable in outlining the ABPN's current policies, training requirements, and other items of interest.

COMMITTEE ON CERTIFICATION IN CHILD AND ADOLESCENT PSYCHIATRY

At its business meeting in February 1991, the Committee on Certification in Child and Adolescent Psychiatry elected the following officers, who began their terms on Jan. 1, 1992: Dr. Theodore Shapiro, Chair; Dr. Thomas M. Haizlip, Vice-Chair; Dr. Lois T. Flaherty, Secretary-Treasurer.

Dr. Elizabeth Weller (Columbus, Ohio) was elected to a 6-year term effective Jan. 1, 1993, to succeed Dr. William H. Sack, who completes his 6-year term on the committee on Dec. 31, 1992.

Members of the Committee on Certification in Child and Adolescent Psychiatry are elected to serve one 6-year term each and are not eligible for reelection. The members of the 1992 committee are Dr. Walter R. Anyan, Jr. (representative from the American Board of Pediatrics; term expires Dec. 31, 1994), Dr. Mark J. Blotcky (term expires Dec. 31, 1997), Dr. Lois T. Flaherty (term expires Dec. 31, 1993), Dr. Thomas M. Haizlip (term expires Dec. 31, 1995), Dr. Kenneth S. Robson (term expires Dec. 31, 1994), Dr. William H. Sack (term expires Dec. 31, 1992), and Dr. Theodore Shapiro (term expires Dec. 31, 1993).

Examination

At its Sept. 20-22, 1991, examination in Baltimore, the Committee on Certification in Child and Adolescent Psychiatry examined 342 candidates; 205 (60%) passed, 58 (18%) conditioned, and 79 (22%) failed or failed/must reapply. Additional statistics are given in table 3. The 1992 examination will be held Sept. 11-13, 1992, in Chicago. The 1993 examination will be held Sept. 10-12, 1993, in Raleigh-Durham, N.C. Applications are due by the May 1 preceding the examination and are available from the American Board of Psychiatry and Neurology, Inc., 500 Lake Cook Rd., Suite 335, Deerfield, IL 60015.

The current fees for examination are as follows: application fee=\$300, oral examination fee=\$600, oral reexamination fee (condition)= \$400, oral reexamination fee (failure)= \$600, written examination or reexamination fee=\$300.

With their applications applicants are required to submit copies of current license registrations showing expiration date, in addition to documentation of all training, photographs, and fees. Training documents must include the exact dates of training. All licensing and training requirements must be met before application for examination.

Committee Decisions and Items of Interest

1. The committee is exploring formats for the recertification examination.

2. The committee continues to arrange examinations following the weekend format. This format has been well received by the host facilities and an overwhelming majority of candidates and examiners.

3. The committee continues to note difficulties with certificates issued to residents. If child psychiatry training is done during general residency, it must be designated as such.

Presidential Address: Reflections on Humane Values and Biopsychosocial Integration

Lawrence Hartmann, M.D.

To realize the relative validity of one's convictions, and yet stand for them unflinchingly, is what distinguishes a civilized man from a barbarian.

—Alexander Herzen, quoted by Isaiah Berlin (1)

It is an honor to be APA president and to address you all. It is a pleasure to be surrounded by family and friends and colleagues. Many of you have helped me, inspired me, challenged me, given me pleasure, given me strength, and taught me, in countless ways over many years, and I am very grateful.

I have had an exciting year. But then, reading and hearing past addresses by APA presidents suggest that many years are exciting. There is continuity and development, but also adventure and individuality and play, in APA psychiatry, as well as in APA presidents.

I hope there has been some adventure, individuality, and play in my presidency, and I hope there may be some in this opening session speech; and that of my distinguished successor, Dr. English.

People sometimes ask me about the relationship of APA presidents to their immediate predecessors, and to their immediate successors, and to the APA medical director (the medical director stays, some of us have noticed, while presidents come and go); also to the Speaker of the APA Assembly, to the members of the Board of Trustees, and to APA senior staff. There are opportunities for covert and overt power struggles, rivalry, narcissistic assertiveness, and corrective overcompensations. There are possibilities for blandly dissolving into a group. But there are also opportunities

for friendship, and fun, and stimulating interaction and cooperation—and I am pleased that from my point of view, Drs. English, Sabshin, Benedek, Pfaehler, Robinson, and other current leading APA figures, have been stimulating friends. We have shared major goals and values, have not often felt bad about our real disagreements, and—I think—have enjoyed working together.

One of my pleasures in getting to know Dr. English a bit this year has been in learning from him, and noticing that the fact that he and I are different, in many details, has added interest to my admiration of his cheerful intelligence, his political and economic and organizational experience, his energy, and his commitment to psychiatry.

I hope and expect Dr. English will avoid something I have noticed in myself: a tendency toward a neurosis (not in *DSM-III-R*, of course) specifically designed for the president of APA: I have noticed in myself a frequent idea that a) I am supposed to know all of psychiatry, and b) I am supposed to fix all of psychiatry. Despite reality testing, I have felt guilt now and then that I have fallen so far short at both impossible tasks.

It is quite clear that no one can know all of psychiatry, and no one can fix all of psychiatry—but such tasks can be instructive, and may teach us not just humility, but realism. How much knowledge of biopsychosocial psychiatry do we require of ourselves and our trainees? What solid core of knowledge and experience allows us to respect what variety among ourselves? What is enough to *know*, in this age of subspecialization, booming biology, intrusive economics, subtle psychodynamics, and out-of-control social arrangements? And what is enough for each of us to *do* to try to make things better, for psychiatry and for mental health, and against mental illness?

This is not a happy era for much of psychiatry. It is a good era for brain research, and a hopeful era for psychopharmacology, but a troublesome era for clinicians, for a great many patients, and for public and private funding. In the state where I live, for instance, under the short-term flag of saving money, the state has been re-

Presented at the 145th annual meeting of the American Psychiatric Association, Washington, D.C., May 2–7, 1992. Dr. Hartmann, 120th President of the American Psychiatric Association, is in the private practice of adult, adolescent, and child psychiatry in Cambridge, Mass., and is on the faculty of Harvard Medical School. Address reprint requests to Dr. Hartmann, 147 Brattle St., Cambridge, MA 02138.

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peatedly slicing away mental health funding and service. It is also a tough era for the use of the biopsychosocial model, which is the difficult but solidest scientific model for our field.

It is a challenging era, and APA has worked hard on thousands of issues this year. I have tried to help on many.

In this speech, I will not summarize our era, or even this past year, or even this past year in APA. I will mention a few issues, problems, challenges, and changes; I will repeat, or vary, several of my last year's themes; and I will have as an underpinning of my talk, and relevant to every economic and psychodynamic and molecular biological corner of my talk, my continuing presidential theme: *humane values and biopsychosocial integration*.

E.B. White advised writers to be clear, and not to be afraid of repetition. I sometimes try to follow his advice when offering my presidential theme.

I will start by calling, or recalling, your attention to several papers by George Engel in various medical and scientific journals, mostly in the late 1970s. He says important things well, and is still continually relevant to our field (perhaps in some ways, he is even *more* relevant to psychiatry today). Also, in talking about integrated psychiatry, we ought continually to integrate our past. Adding new data is essential, and often exciting. But just adding data is not enough. We need concepts, and we need integration.

Dr. Engel of Rochester was a major voice—perhaps *the* major voice—a few years ago, saying that the usual biomedical model is inadequate, and that we need a biopsychosocial model. His examples were largely medical rather than specifically psychiatric. His longest case example was an acute myocardial infarction, with a cardiac arrest; in that case, as in others, he demonstrated the efficient relevance of the psychological, the psychodynamic, and the social, to what was, and often is, seen and treated more partially, and narrowly, as one or another physiological disorder.

Engel, in his papers, sees medicine in the 1960s, 1970s, and 1980s, as not biopsychosocial enough, but says that *psychiatry* is relatively good at being biopsychosocial. I worry, as you will notice, that in 1992 even psychiatry is not biopsychosocial enough. In fact, I think psychiatry has regressed from what was a fairly sound, overall biopsychosocial model. Partly because of biological advances—e.g., in neurobiology, psychopharmacology, molecular genetics—psychiatry is in many ways *less* biopsychosocial than it was 20 years ago. As part of neurobiological advances, and the remedicalization of psychiatry—very productive in some spheres—psychiatry and the model psychiatry has of illness and wellness have, it seems to me, shrunk back from biopsychosocial integration toward the narrower, more purely physiological medical model that George Engel persuasively argued was inadequate for all of medicine 15 or 20 years ago.

"The rest of medicine," said Dr. Engel (2), "appears neat and tidy. It has a firm base in the biological sci-

ences, enormous technological resources at its command, and a record of astonishing achievement in elucidating mechanisms of disease, and devising new treatments. It would seem that psychiatry would do well to emulate its sister medical disciplines, by finally embracing once and for all the medical model of disease.

"But I do not accept such a premise," Engel added, "rather, I contend that all medicine is in crisis . . . from the same basic fault as psychiatry's, namely adherence to a model of disease no longer adequate for the scientific tasks and social responsibilities of either medicine or psychiatry.

"The dominant model of disease is *biomedical*, with molecular biology its basic scientific discipline. It assumes disease to be fully accounted for by deviations from the norm of measurable biological (somatic) variables. It leaves no room within its framework for the social, psychological, and behavioral dimensions of illness" (2, pp. 129–130).

Engel (3) said that "Rasmussen traces the philosophic origins of this [the biomedical] model back three or four centuries when established Christian orthodoxy lifted the prohibition against physicians dissecting the human body as long as they did not presume to deal with man's soul, morals, mind, and behavior This compact helped determine that Western Medicine be based upon dualism and reductionism Dualism predicates separation of mind from body. Reductionism assumes that the understanding of a more complex entity can be best achieved by its analysis into its component parts and therefore that the complexities of life and biological phenomena, including behavior and mental processes, are to be studied and explained by the methods and in the language of physics and chemistry. Reductionism fosters a view of nature as involving interactions of discrete entities in a linear causal fashion, simple cause-and-effect relationships. This influence is expressed in the habit of speaking of diseases not as dynamic processes but as discrete entities, the elimination of which awaits only discovery of their causes" (3, pp. 156–157).

"The biomedical model," said Engel, "has been extraordinarily fruitful. But this very success has served not only to entrench dualism and reductionism but also to encourage its more enthusiastic advocates to promote the biomedical model as ultimately capable of explaining all aspects of health and disease. The dogmatism inherent in such blind faith in and exaggerated claims for the model has been a powerful factor in deflecting scientific interest and attention from problems that do not readily yield to the biomedical approach. Outstanding among these have been the more personal, human, psychological, and social aspects of health and disease" (3, p. 157).

"Nothing exists in isolation. Whether a cell or a person, every system is influenced by the configuration of the systems of which each is a part, that is, by its environment Neither the cell nor the person can be fully characterized as a dynamic system without characterizing the larger system . . . of which it is a part" (4, p. 537).

Engel points out that some shifting from the biomedical to the biopsychosocial model *has* been successfully tried now and then, as prominently at Hopkins at the time of Adolf Meyer, and at Rochester more recently.

"The biomedical model is disease oriented" but "not patient oriented," said Dr. Engel (3, p. 158).

That is true. It is even convenient. But I would argue that particularly in the area of psychiatry, the biomedical model is usually not even fully or competently disease oriented.

I think much of George Engel's writing on medical models is pointedly relevant today, to good clinical care, good service delivery and planning, good teaching, good research, good prevention, and good long-term politics and economics.

Yet, Dr. Engel's point of view has formidable opponents in the political and economic forces in and around psychiatry today, and in many who like and respect and do biological psychiatry.

We psychiatrists, with our recent and continuing excellent but unbalancing advances in brain biology, and with our influential shift toward the relatively superficial and undynamic *DSM-III* and *DSM-III-R*, would do well to take Dr. Engel to heart.

Before going on to a few words about *humane values*, and about new science; splitting of psychiatry; managed care; universal access; human rights; children and adolescents; and a few other issues—before all that, let me add an example of new scientific research that I think may help some of us think biopsychosocially. Last year, in my president-elect's speech, I used the *clinical* example of a child patient who had diagnostic and therapeutic issues that demanded simultaneous thought and therapeutic action in biological, psychological, and social fronts. Less would have been bad psychiatry. There are thousands of patients I could point to as lively parallel examples. In fact, *all* patients I have ever seen seem to me best looked at biopsychosocially, even if likely strategies for understanding and helping one may be more in one realm, for another, more in another. All patients—an abused child, a drug-abusing teenager, a neurotic graduate student, a schizophrenic adult, a depressed elder, an AIDS patient, a homeless patient—all patients deserve integrated biopsychosocial understanding and help.

But that is human patients. Here, briefly, to make a biopsychosocial integration point, I want to compare you all to . . . aggressive fish.

You may wish to resist the comparison, or you may not. And I apologize that the following research was done only on male fish. I expect that there are, or soon will be, comparable studies on females.

Dr. Russell Fernald, a Stanford neurobiologist, has been studying the African cichlid fish. He has discovered that how a male cichlid interacts with other males, and whether it is socially dominant or meek, not only has a major effect on the fish, but *changes the brain cells* in charge of the fish's size, color, and capacity to reproduce.

In aggressive male fish, commanding large territory, brain cells in the hypothalamus are six times larger than

are equivalent cells in milder mannered males. Further, the dimensions of these cells are plastic: should the aggressive fish meet a larger and/or more aggressive fish, the hypothalamic neurons of the defeated male will rapidly shrink. After the hypothalamic cells have shrunk, the male's testes follow suit, decreasing the fish's apparent desire and ability to breed. In the laboratory, some male fish were *environmentally pushed* from dominators to meek types; some from meek types to dominators. Their *cellular changes followed*. When a dominator emerged socially, he began to flaunt his success: physical changes began; he grew bigger and his coat brighter; his gonads swelled, and started making sperm.

Dr. Fernald found that key behavioral changes occurred first, and drove the brain changes. The dramatic growth in brain cells that produce gonadotropic-releasing hormone followed environmental change; and testicular and color changes followed that brain cell change.

Social change alters brain cells.

That is not a great surprise, but it is a relatively tidy research demonstration of what many of us who think biopsychosocially assume is routine interaction of brain and mind. We usually do not, however, have tools with which to measure such changes in vivo in humans. In fact, you might note that given our access to somewhat different aspects of fish than of humans, the *psychological middle ground* is not prominent or explicit in this fish research. (How does the fish feel or think about all this?) The demonstrations relied largely on the anatomical/physiological and the social, with the psychological middle level of description merely implicit.

With better (and less intrusive or harmful) tools (as, for example, some of our new neuroimaging techniques), we already are to some extent, and soon will be to a greater extent, able to demonstrate many similar bits of biosocial and biopsychosocial continuity in humans.

Enough about fish. I would, after all, like you to notice not just biopsychosocial integration but also humane values.

Good clinicians live by humane values and biopsychosocial integration.

Humane values require us, in promoting mental health and fighting mental illness, to be aware of and care for and treat *whole people in context* and *over time*: whole biopsychosocial people in context and over time. Some of you may realize that this requirement is right but also a bit nostalgic, and sometimes impossible. So it is. Many goals and standards are. Some of you may also realize that child psychiatry is traditionally closer to this ideal than adult psychiatry is—and that may create some useful tension in your minds, because child psychiatry has also traditionally been *less* good at acquiring a base of crisp, quantifiable research studies.

Humane values require doing, teaching, researching, preventing, and, in the real world, getting involved in some political and economic and public affairs areas on behalf of mental health. Humane values require us to fight stigma (and APA may have helped make some

gains here in recent years). Humane values should also lead us to special interest in the underdog, and those who are different. In my case, this has involved international affairs and ethics and human rights and child psychiatry. But in all our cases, it should involve interest in the old and the young, in cross-cultural psychiatry, American Indian issues, black issues, Hispanic issues, Asian-American issues, gay issues, and women's issues. To be humane to ourselves, we all have to select some areas of special interest, but we can retain an active view of the whole field around our expertise.

We each know that we cannot know all of psychiatry, and that increases in the field's knowledge can seem in a general theoretical way welcome, but in a personal way, burdensome. It is hard to keep up. We may even resent some of our colleagues who do keep up, at least in some areas; and probably many of us are tempted to resent or even reject colleagues who know and do different things.

Reasons for splits and reductionism are many, but in addition to economic pressures, and unbalancing advances in measurable and published research in one or two sectors of our field, we may be tempted into reductionism by unacknowledged frustration in a field that seems too big to master, and too bedeviled by outsiders who push us, and sometimes pay us, to simplify. Even if we know with our heads that integration plus cross-fertilization of new with traditional areas of psychiatry is right, many of us are now guilty of biological reductionism, just as some of us are, and more of us recently were, guilty of environmental or psychodynamic reductionism.

Some psychiatrists, and patients and others, now think of psychoanalysis as irrelevant and passé. Some psychoanalysts and psychotherapists, and patients, now think of psychiatry as hopelessly biologically reductionist. Some psychiatric residencies now hardly take psychodynamic psychiatry seriously.

I used to think that psychiatrists characterologically tolerated and liked and respected complexity—as opposed for instance to some surgeons, who often seem to me to want to cut decisively through all tissues and issues. But in a time of scientific complexity and economic frustrations, I have met a good many psychiatrists who seem to yearn for simplicity.

I make a distinction between clarifying, which is usually a virtue, and simplifying, which is often not a virtue.

There is also a tendency in complex fields, or eras, to split off parts (and sometimes to master them, or at least label them). Subspecialization in psychiatry is here, and has many advantages. But good subspecialization should retain awareness of the whole field. Creating subspecialty expertise is fine, but implying that there is reality, as opposed to marketing usefulness, in spinning off a new so-called "clinic" for each of one or two or three dozen *DSM-III* diagnoses, is going a bit far (and reminds me of the early twentieth-century habit of labeling hundreds of separate phobias, each neatly in Latin or Greek. I particularly liked *triskaidekaphobia*).

Splitting is here. Splits are here. Some famous splits

in psychiatry have depended on personalities in conflict, but many have developed in response to different access to different data, or different understanding of different data.

New data are abundant in our complex and lively field, but there is relatively little agreed upon integration of the biopsychosocial data. That contributes to a split between researchers and clinicians; between or among more biological, more psychological, and more social psychiatrists; and between those most interested in severe and chronic mental illness (e.g., psychoses) and those most interested in the larger number of people with mild to moderate mental illness (e.g., character disorders and neuroses). The last split, like some others in American psychiatry over the past 25 years, has probably grown, and not just as a reasonable or proportionate response to previous overenthusiasms or to good new knowledge.

There are currently major pressures on us to widen the split between severe mental disorders and mild to moderate mental disorders. Money pushes the split wider in several ways, including pressures from insurance and managed care and others to see only what is physical as real, to reduce psychiatry to acute care, to medicate symptoms rather than treat patients; and also including large pharmaceutical company support for some kinds of psychiatric understanding and treatment, but far less, if any, for other kinds.

In several courts and state legislatures, and in several insurance plans and regulations, there have been efforts to ensure that if and only if a mental illness has a demonstrable organic component should its treatment be covered well, or at all, by insurance. That is an interesting splitting dilemma for psychiatry.

In a climate of routine discrimination against coverage of mental illness, the California Psychiatric Society, for instance, has chosen to try to get better insurance for the most severe mental illnesses by asking that those, but not other mental illnesses, be covered parallel to physical illnesses.

The Alliance for the Mentally Ill, a large and effective group mostly of relatives of severely mentally ill people, very much favors this approach, and wants to fund and develop the biological end of the biopsychosocial spectrum, while caring little about, and often disparaging, psychodynamics, psychotherapy, and the psychosocial areas of mental illness.

Similarly, far from California, a New England legislator, much influenced by the Alliance for the Mentally Ill, has just taken a similar tack, with considerable skill and success in Maine. She argues that getting good coverage for what she defines as more or less "real," that is, "physical" mental illnesses, is good in itself; and could be a way of getting the camel's nose of psychiatric diagnoses into the tent of nondiscriminatory coverage. I am afraid it is far likelier to let a few in and keep most out, and even to increase splitting and infighting among the mentally ill and their advocates and helpers. Rather than a part of one camel with one body, the mentally ill are millions of separate, relatively weak people, rela-

tively easy, on multiple grounds, to separate and keep out. It is somewhat analogous to a bunch of sophomores getting into a club and keeping fiercely out a lot of other sophomores, and the larger group of freshmen or freshmen women.

Tactics get argued about, but I think we need to work for good insurance coverage of *all* mental illness, as much as possible on a par with coverage of physical illness. I expect that *all* mental illness has physical correlates in the brain, even if so far we are only beginning to be able to demonstrate a tiny edge of these, and even if demonstrating brain correlates does not validly demonstrate severe or meaningful illness.

Problems with boundaries of insurance coverage have significantly affected definitions and concepts and boundaries in psychiatry. Psychiatry that is interested only in psychosis, and in the most severely ill, seems to me a bad retreat to the late nineteenth century. Despite its tactical helpfulness to some patients in the short run, it is, I think, strategically unwise in the long run.

We have learned in this century a great deal about psychology, psychodynamics, development, family therapy, social psychiatry. Also a great deal about prevention, a politically difficult and vastly neglected field. We are currently losing some of that, and we should fight to reverse these losses. Those areas do not contradict biological, physiological psychiatry. The areas in most ways complement one another.

We need continued integration of biopsychosocial knowledge. Who is going to do that? Can we expect our trainees to do it if some of us do not do it well ourselves?

The whole area of bio versus psycho versus social will probably remain central to psychiatry for a while, and an area where we are at risk of major premature closures. One could call the risk intellectual and clinical segregation rather than integration.

Can we cooperate? It is easy to denigrate those who think differently, or who know different things. Psychiatrists do this to psychologists, but also to psychiatrists, to neurologists, to internists, and to many others. Some simplification, for a while, for a purpose, is often essential and productive, e.g., for some clear research. But in a complex field, with many simultaneously active variables, and different levels of research and clinical access, continual back and forth motion between analysis and synthesis seems to me essential. So does some *extra* effort to study what is *hard* to study and *long* to study, not just what is relatively easy and fast to quantify and publish. Cooperation and tolerance of complexity seem to me hard but essential in a complex field like brain plus mind plus influences on brain and mind that result in health and illness.

Clinicians accept imperfect complex approaches and approximations, educated guesses and re-guesses and syntheses and summaries, often nowadays informed by considerable education not just in psychodynamics but in medicine, genetics, brain physiology, psychopharmacology, developmental psychology, family dynamics, and some sociology and anthropology.

That is clinical psychiatric integration.

Many researchers, as opposed to clinicians, are impatient with much of this, and for their good reasons want to isolate factors and measure crisp, measurable units. They have made and will make some brilliant advances. But psychiatry remains at some risk as a science, and as an insurable medical specialty, partly because its complexity makes it a major example of a general problem in science: what is easiest to measure tends to get measured and called real, or important; what is harder to measure, even if as important, or more important, gets dismissed from reality, and gets measured and valued far less.

At a health-care economics symposium this year, someone claimed that by saying this, I am against measurement. Not at all. That is a mischievous and perhaps defensive mis-hearing. What is easier to measure gets measured far more, and that is a complex danger for psychiatry.

Good long-term studies are few. Good integrative studies are few. Good studies of psychodynamics and psychotherapy are very few, and those few tend to be narrow and short-term.

It has been calculated that to do good controlled studies of psychotherapy of the major *DSM-III-R* axis I diagnoses would take decades, and billions of dollars. That does not mean such studies are not important. But, badly as we need some such studies, it does mean they probably will not be done. And that leaves us relatively vulnerable, and open to being run by nonclinical simplifiers.

DSM-III and *DSM-III-R* and *DSM-IV* inevitably come into this discussion, as they are useful to nonclinical simplifiers. Part of the movement toward reliable categorization and measurement, they have helped many aspects of psychiatry, but harmed many others. They emphasize clarity and reliability, but sacrifice validity and the whole person. There are vigorous signs of diagnostic life outside of *DSM-III-R* axis I—e.g., complex interest in axis II; in axes III, IV, and V; in possible added axes; in etiology; in comorbidity and dual diagnoses (which are now ubiquitous and slippery); in reactive disorders; in psychodynamics; in development and adaptation as part of diagnosis, especially in youngsters; in family and social stressors; in protective factors.

All these persist outside *DSM-III-R* and *DSM-IV*. Life is complex. Clinicians integrate what we can.

Perhaps in some ways similarly, at different levels, organizations like APA integrate what we can, even if there are always hundreds of simultaneous issues to work out. As last year in this setting, I can barely begin to list, much less discuss, all that APA does in a year. For a good summary, including good notes on APA activity with the resource-based relative value scale and Medicare, I refer you to recent APA staff summaries, and to the annual Medical Director's report. But before ending with a few words about children, I would like briefly to touch three topics that members around the country have talked to me about repeatedly: managed care and universal access; psychologists; and ethics.

Managed care, variously defined, is a huge concern, very much here, and popular with many in government and business. It is not at all popular with many—probably most—psychiatrists. I think many psychiatrists hate it, and feel terribly worn down and wasted by it. And as to patients and the public, they are mostly still not yet sufficiently aware of or educated about it. Quite aside from its many conspicuous abuses, such as wearing down clinicians by harassment and paperwork, it is driven by a large interest in *cost cutting* (not quality enhancement) as the ruling concern; of *shifting power* away from doctor, and patient, to third and fourth parties without medical degrees; and of *overruling what is best for an individual* patient with what someone thinks is good for a larger entity (at best, society, but very often just a managed care or insurance company's short-term profits). These driving interests are often disguised.

Managed care has private and public arms. It is part of the current inherently flawed push to "privatize" public psychiatric programs, and is nearly certain to be, in some form, part of any universal access to health care plan for the United States. Universal access is long overdue in America, where tens of millions of us are currently left out of our health nonsystem. Access should include *as much as possible* mental illness care coverage, *as equal as possible* to physical illness care coverage. Canada and Germany are highly useful models, despite propaganda to the contrary. It is not just mental illness but all health care that is not well covered in the United States. And capitalism, to the surprise of some Americans, survives in the vast majority of industrialized nations, all of which have universal access to health care. This year there are being discussed in Congress a dozen or so major universal-access-to-health-care plans, proposed by major organizations and by some members of Congress. One gathers that not one of these is likely to pass this year, but we are getting closer.

Universal access is overdue, but managed care (even the rare best of managed care, run with legitimate physician peer review) is not "the answer" to high health care costs. It can contribute at best a moderate part of an approach to high health care costs, though its aggressive use of businesslike vocabulary often implies or claims much more.

I do not think our health care costs are too high in America. We spend about as much on alcohol and tobacco, for instance, as we do on health care. In fact, I think we probably spend too little on health care. (What an eccentric I am!) I think that guns and butter should be a major issue to anyone interested in health and mental health, and I think America vastly overspends on military matters, and underspends on investing in people and health. But to persuade the American public, the American government, and the American business establishment to change values, and spend less on the military and more on health, will require major work.

Then psychologists. Are boundaries possible? We go on being uneasy allies, with some big disagreements that get in the way of potential cooperative work. Are

the noisiest disagreements really turf wars, or are they legitimate safety and quality-of-care-of-patient issues? Can we as professionals insist on any standards, or are all *standards* thought to be undemocratic, or greedy, or violations of antitrust laws? Nearly all psychiatrists I have heard from, and a gratifying number of psychologists, agree with my last year's Boston-influenced slogan: No medication without medical education.

Then ethics: Despite America's widespread assumption that ethics means sex, ethics does not at all mean just sex. It means good and decent behavior, good professional behavior, good care. Ethical questions around money, for instance, and responsible inpatient and outpatient practice decisions, certainly including managed care, are currently lively. But for posterity's sake, I would like to record that perhaps never in the history of the American Psychiatric Association has an APA president been called upon to spend so much of his time considering psychiatrist-patient sexual contact as this year. There has been much publicity about several cases, much of it feelingful and inaccurate—as news coverage of sensational topics often is. That the great majority of psychiatrists behave well and safely, and work hard never to harm their patients, does not quite protect us. APA and the public are rightly concerned about the issue, and clear as many of us think our ethics code and procedures are, we clearly need to do better. That will include prevention and education; openness; clear and firm standards; and due process, including punishments, to uphold standards. We have much of this in place now (far more than the media usually acknowledge, and far more than the public and many of our own members know, and more than any other national professional organization that I am aware of). Yet we need to do more, greatly to reduce bad behavior and to demonstrate that part of profession is to have and insist on clear, high, ethical standards.

Let me end, as I often do, with a few words about children. I regularly introduce children into my remarks on humane values and biopsychosocial integration because I like to work with, and teach about, children and adolescents as well as adults; but also because it seems so clear to me that child psychiatric pathology and health, including severe pathology, and even in the minority of cases, where there are demonstrable organic problems—child psychiatric pathology and health are very dependent on family and environment, i.e., on the social end of "biopsychosocial" that is so often left out of 1992 psychiatric discourse.

I recommend to you David Hamburg's new book, *Today's Children: Creating a Future for a Generation in Crisis* (5). Among the advanced countries of Western Europe and Japan, Hamburg says, "the United States now ranks in the bottom quartile in caring for children." He says that the United States is committing "atrocities," and that we have already lost a substantial portion of the generation of children under age 16. His book is full of sad facts, but also of psychiatrically educated suggestions, especially for prebirth and infancy, and the junior high school years.

Do we as a society particularly dislike children? Probably not. But we pretend to like them more than we do. And, as I frequently point out, children don't vote. They are poor. They lack some mature political skills. They depend on others. And they are rarely desperately and immediately scary to adults. Short-term thinking—which most politicians are best at—allows us to ignore and shortchange children and adolescents, and thus our own field and our own future.

All the statistics that I cited last year on abuse and neglect and foster care, and homeless and at-risk and psychiatrically disordered children, remain similar or worse.

Twenty percent of United States youngsters live below the poverty line. In cities, 30%. Among Hispanics, 39%. Among blacks, 45%.

The numbers of children in our very flawed and unsafe system of foster care is still about 350,000, and the number of homeless youngsters is still around 200,000; 7.5 million children still need treatment for diagnosable mental disorders.

Unwed teenage pregnancies still are an epidemic in the United States: every year, about one million unwed teenage girls, about one in ten every year, become pregnant. The rates of births to unwed teenagers, most destined for poverty and major additional problems, have about quadrupled in the past 25 years. Not just abortion information, but even more basic and less controversial *prevention* education—to prevent both pregnancy and AIDS—is severely and shamefully hampered and blocked in the United States. Teenage drug and alcohol use rates are still huge (even if cocaine may have peaked), and every year 2.5 million teenagers contract a sexually transmitted disease—which by now implies not just visible disease, but a very large pool of so far undetected HIV-positive teenagers.

And violence? Rape and murder rates are staggering. Teenage violence is taken for granted in America today, but it increasingly involves guns and death (and the United States has a limp lack of social policy to deal with this). The average American 16-year-old has seen 100,000 acts of violence on television. On the average day, 135,000 youngsters bring guns to school.

There are, I recently learned, 200 million guns scattered about the United States; and gun merchants worry that the market is slowing down. And, a quieter little statistic, how many people are licensed to sell guns in

the United States? 270,000. Guns are cheap and technically terrific. A 13-year-old holding an Uzi submachine gun has little understanding of his own mortality, let alone your mortality or mine—but as a slum teenager who had shot at and, he thought, hit people, said, “they were just people.” “It’s like an article of clothing . . . I put on my pants, my shirt, my hat, and my gun.”

Social policy and family policy are intricately tied to child and adolescent health and mental health. Social policies do not rest on perfect proofs, but on wisdom and experience. We have much wisdom and experience as to child rearing and preventing problems and fostering strengths in young people, and we are ignoring much of our own wisdom and experience, and not fighting for it. Psychiatry can and should contribute to reasonable, decent, educated social policy.

As I look back on a good year of hard work, and since I will at the end of this week shed the exciting honor and somewhat charmed life of an APA president, I feel a bit like Prospero at the end of *The Tempest*; not yet old, but giving up his wand and magic powers, and returning to a different reality:

Now my charms are all o'erthrown
And what strength I have's my own.

I urge you all, whatever your roles, whatever you do, whatever your particular skills and interests, whether you are clinicians, researchers, teachers, students, administrators, whatever—all of you—I urge you to invent ways of applying your talents and energies in some ways that will help biopsychosocial integration, that will help humane values, and that will help children and adolescents grow mentally healthier than they now are in America. Thank you for listening.

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Response to the Presidential Address: Patient Care for the Twenty-First Century

Joseph T. English, M.D.

Dr. Hartmann and I have enjoyed an extraordinary relationship over the last year. We hardly knew each other before it became my task to assist the efforts of his presidency. I think we have agreed on nearly everything, which is quite remarkable when you consider that we are both quite opinionated. The only lapse was when he once suggested, while addressing a meeting, that the Irish could be wrong about something. I don't think he realized, at the time, that English is Irish. But we have been able to straighten out even this problem. I was quite sure of it when he wore an emerald green tie to the reception that evening.

In some way, I think this incident captures the essence of Lawrence Hartmann's presidency and the powerful impact it has had. We are a most diverse profession, and that diversity is our strength. Dr. Hartmann's theme, celebrating the humane values that bind us together as a profession as well as the balance and tolerance we achieve through the concept of biopsychosocial integration, is precisely the message we need to hear in these turbulent times. As the most tolerant of the medical specialists, we must be understanding of each other and in our practice. In this he has provided superb leadership and example.

As an illustration of this, Dr. Hartmann was able to bring together the elected leadership of APA and of the American Psychological Association for an unprecedented full day meeting. There is a rumor that the Secretary of State tried to reach him for advice after that feat. Just this week, the two APAs met with the leadership of the American Nursing Association and the National Association of Social Workers. Under Larry's leadership, it was clear where we disagreed, but it was made increasingly clear where we could collaborate for the sake of our patients and in the public interest. And he did this as he has done so many other things for us, with warmth and wit, with scholarship and sophistication. His distinguished parents would be proud. And we are grateful.

But I now remind myself that, above all else, the

President-Elect should be brief. I cannot afford to have my judgment questioned at the inception of my term.

Let me tell you of my hopes and aspirations for the year to come.

My choice of theme complements Dr. Hartmann's. I chose it after consulting with hundreds of colleagues, some of whom wrote to me eloquently, and many of whom are in this audience tonight. For this help, I am grateful.

My theme for the next year will be Patient Care for the Twenty-First Century: Asserting Professional Values Amidst Economic Constraints.

As the twentieth century draws to a close, we find ourselves in the midst of the most important health policy debate since the decade of the 1960s, which gave birth to Medicare and Medicaid and the beginnings of public insurance for all in need of medical care in the United States. This was a generous period in our nation's history, when we dared to think that access to health care was an entitlement, derived from the right to life itself.

We now find ourselves in a different time, when the question more often involves the triage of human life. The physician is asked to decide who shall receive care and who shall not. Soon it may be a question of who shall live and who shall die. After all, society has other needs and health care has become a favorite target for cutting costs. In these times we are told that we need "managed care." How ironic. Psychiatrists have joined together to manage the care of patients in the United States for 148 years; it was that long ago that we became the first of the medical specialties in the United States to organize a medical association to advance this important work. We will soon celebrate our 150th anniversary in Philadelphia, where our founder, Benjamin Rush, was organizing care for patients with mental illness even before we had become an independent nation.

What we are really being told is that others want to manage the care of our patients, but not necessarily in the tradition of Hippocrates. There are stockholders to be considered, the competitiveness of American business, the federal deficit, and public and private budgets to be balanced. In the process, we find that many of our patients are excluded, and that even more are being placed at risk.

Jay Cutler will tell you that there is no health reform initiative under consideration by Congress in which our patients and our practice are not at risk. In many of

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them, mental illness is not mentioned at all. With our powerful and effective government relations organization, we react to such challenges brilliantly, and often successfully. But these times require more and demand the efforts of all of us.

At the midpoint of this century, a group of psychiatrists came back from extraordinary service in World War II and saw a time of opportunity. Their names are legend: Braceland, Ewalt, Menninger, Felix, Grinker, Sullivan, Appel, Tarjan, to mention a few.

They convinced President Eisenhower and the Congress of the United States to embark upon a great study of the mental health needs of our people. They hoped that World War II would be the last war and that we could apply the lessons they had learned to radical improvement of mental health services here at home. Their leadership brought about the Joint Commission on Mental Illness and Health. This commission included all of the mental health professions together with citizen organizations—and the American Psychiatric Association played a crucial leadership role.

The product of their work was given to a new, young President, John Kennedy, who in 1963, shortly before we lost him, sent the first message to Congress on mental health and mental retardation, outlining a plan of legislative action to benefit the mentally ill and the mentally retarded. This work laid the template for mental health services for the remainder of this century.

But it also left much to be done.

It is time for us to begin a similar effort to ensure the well-being of our patients in the twenty-first century, with the same commitment and dedication and with a much greater chance for a century of peace in the world than our predecessors could ever have envisioned.

To begin, I plan to ask the Board and Assembly for their authorization to initiate a process of strategic planning for APA and to engage the talent we need to assist us. Such a process will go beyond reacting to the crises of the moment. It will help us to set goals and priorities to debate the crucial options, to develop action plans for implementation, with accountability to the membership should we fall short. I have chosen three major areas for the initial engagement of this process.

The first is health policy. Our goal will be to ensure that the needs of our patients are met. But we must define those needs clearly and precisely and develop short- and long-term objectives to address them. We will have to make some tough choices, because in these times you can't have it all. Bob Gibson, who did so much to guide our economic initiatives in the 1960s, has accepted reappointment as leader of the Council on Economic Affairs and has accepted a major responsibility in the development of this strategic plan, together with John McGrath, who has agreed to continue as chair of the Joint Commission on Government Relations, with Steve Sharfstein and Don Scherl, with Jay Cutler and his staff, and with the leadership of the Board and Assembly. The planning for this effort is already underway; the first meeting is scheduled for July 1992.

Richard Surles, Mental Health Commissioner of the State of New York, has agreed to help us reestablish our historic community of interest with the states and to develop the new definition of public/private partnerships that the new century will require. The National Institute of Mental Health has already offered us its resources and participation. The Hastings Institute, with a similar effort already underway, has agreed enthusiastically to collaborate with us. And, as we develop our plan, we shall reach out to the other mental health professions, to our colleagues in organized medicine, and especially to patient and citizen organizations.

All of this is being coordinated by the master strategist who is our Medical Director, Mel Sabshin. How fortunate we are to have his wisdom and experience to guide this important effort.

Our developing product will be shared with the membership at every opportunity, but especially during our Institute on Hospital and Community Psychiatry in Toronto and our next annual meeting in San Francisco.

The process will be participatory, and its spirit should be that of a little-known Peace Corpsman from Pennsylvania, who took the issue of health care to the people of his state, winning election to the U.S. Senate despite incredible odds and making his state and the nation awaken to the political importance of health care as an entitlement. And when Harris Wofford heard in his suite that he had done it, your President-Elect was there and was the first physician in this country to offer him congratulations on your behalf. We have friends, and we must help them with our planning, and they will help us.

The second area is the recruitment of young talent to our profession. There is no need to plan for the future if we do not attract the young to join our ranks in the present. Here we have our work cut out for us. The 30% decline in medical students entering psychiatry's match this year should galvanize us to action.

The appointment of a director for APA's Office of Medical Education shall have my highest priority. In addition, I intend to meet with the academic chairmen of our field, a powerful and talented group, to urge them to place an even greater emphasis on undergraduate medical education and on efforts to attract talented medical students to psychiatry. Our reach must extend into the liberal arts colleges and into the high schools of our communities as well.

We have succeeded in celebrating our science, but there are other aspects of psychiatry's mission that will also appeal to the young, and we must rediscover this message and work energetically to deliver it.

I am delighted to report that James Shore of Colorado has accepted the leadership of APA's Council on Medical Education and Career Development and will lead the effort to develop our strategic plan in this area. No one in APA is better equipped to provide us with leadership in this crucial area.

The third area for action is the public perception of psychiatry. When the film that wins all the major Academy awards is about a psychiatrist who eats his pa-

tients, we have a problem. When in many other films, psychiatrists are having sex with patients; when all of this is not just going on in the movies; when such abuse is the subject of a cover story in *Newsweek* and lead stories in major newspapers, magazines, and public television documentaries (two on network television in a period of 10 days); when we are called bounty hunters and kidnappers of patients in Congressional hearings, we truly have our work cut out for us.

We know that we are much better than that. It is a small fringe of our profession who are involved in such abuse. We should be proud that no specialty of medicine has worked harder to enforce the code of medical ethics. We know that we have incurred enormous expense to remove or suspend for ethical abuse more than 100 members of APA over the last 10 years, always with careful attention to due process and good procedure, but we must also ensure that the public knows it and appreciates our continuing commitment.

I am delighted to report to you that Edward Hanin has agreed to chair APA's Joint Commission on Public Affairs and is already hard at work on the development of a strategic plan for new initiatives in this area. Also, I am grateful to the Board for approving a waiver so that the splendid leadership of our Ethics Committee may be continued by Jeremy Lazarus over the next year. Having spent two days with this committee under Jeremy's leadership during its recent meeting, I can personally attest to the quality of their work and the service they render our profession. But we must ensure that knowledge of our ethical code by the membership and the teaching of it to our medical students and residents receive a new priority and emphasis. Dr. Lazarus will give us superb leadership in this endeavor.

Clearly, all of this is interrelated. We shall succeed in the political process if we retain the confidence and support of the public. To maintain this confidence, we must demonstrate a renewed and highly visible commitment to professional and ethical values. Nothing could help more to maintain and enhance the public perception of psychiatry. And such efforts will help us to attract medical students to our field.

Because of what has been happening in many of the cities we left to come to this meeting, may I leave you with a few additional thoughts.

More than 200 years ago, Benjamin Rush was asked to lead a small planning group to develop some working papers, which were then given to Thomas Jefferson. Jefferson used those papers in writing the Declaration of Independence. The power of those ideas has demolished the Berlin Wall, torn asunder the Iron Curtain, and brought freedom to the people of Eastern Europe. Those ideas now make possible the free practice of medicine and the demise of the abuse of psychiatry by the power of the state. But we need to remind ourselves that the promise of these ideas is yet unfulfilled for many here in our own country.

Twenty-five years ago, in the wake of the riots that

followed the death of Martin Luther King, President Lyndon Johnson appointed the Kerner Commission to make recommendations that would avoid another such a national tragedy. He asked a psychiatrist, Walter Menninger, to serve on that commission. And we should recall this evening what the Kerner Commission said then, and I quote, "Our nation is moving towards two societies, one black, one white, separate and unequal." The tragic events of the last few days make these words crash back into our consciousness as never before. But even more importantly, we should remember that a war on poverty was declared and that programs like Head Start, Neighborhood Health Centers, Foster Grandparents, the Job Corps, and Vista began to flourish all over the land. And psychiatrists helped with all of these efforts. We also had the Peace Corps, ably led by Sargent Shriver, the commanding general of the war against poverty. But sadly, another war retarded the efforts of the war on poverty, leaving much yet to be done. On this first Sunday in May, which national leaders have asked to be a day of reconciliation, let us enter into that spirit and join with those who say that it is time to make a new beginning.

As APA initiates its planning process for the twenty-first century, let us work and plan for public mental health in the largest sense. Public mental health should involve more than reimbursement and economics; it should include how we do our part to help end the plague of racism and alienation in this country through a new understanding of what "one nation, indivisible" is all about.

Our patients come first, but they need more than treatment. We must be interested in catchment areas, but our concern should be that they become caring communities. We should never return to the days when our reach exceeded our grasp, but that does not mean that we should fear to reach out with our professional skills and commitment when our help is needed.

I spoke to Gary Tischler, Chairman of the Department of Psychiatry at the University of California in Los Angeles, at a symposium honoring Danny Freedman. Dr. Tischler told me that his department has already been asked by the public school system in Los Angeles to participate in efforts that would help schoolchildren understand what has just happened in their city. The faculty of his department drew straws to see who would come to Washington for our meeting and who would stay behind to plan this help. Let us look for such opportunities and offer assistance even before we are asked.

When we gather in San Francisco next May for our annual meeting and review our strategic plans for patient care in the twenty-first century, let us also be prepared to tell each other tales of how we labored during the year to promote understanding of what "one nation, indivisible" is really all about.

I look forward to working with you in the year before us. Thank you.

Lawrence Hartmann, M.D., One Hundred Twentieth President, 1991–1992

Melvin Sabshin, M.D.

Our 120th President, Lawrence Hartmann, is an extraordinarily *cultured* man. His theme, Humane Values and Biopsychosocial Integration, is profoundly autobiographical as well as a credo for the *next* phase of psychiatry and a celebration of what good clinicians do now.

A product of distinguished Austrian families, Larry has had a life history and professional career (or perhaps careers) that are a remarkable integration of diverse forces, paradoxes, multiculturalism, talents, styles, and personal philosophy. It is a special privilege for me to introduce our President. While I have known him for almost two decades, a series of professional and personal events have drawn us much closer during his presidential year. I will always remember the personal warmth and support that emanated from Larry, belying, but also complementing, his austere and *occasionally* royal surface demeanor.

The life stories of past presidents of APA have often been fascinating tales of how outstanding women and men chose or discovered a pathway into psychiatry and rose to leadership positions. Rarely, however, have we had a President whose personal life has intertwined so closely with the history of psychiatry in Europe and the United States and, indeed, the whole world. World War II, its antecedents and its aftermath, changed psychiatry radically. Indeed, in the United States the face of psychiatry altered fundamentally after the war, and the consequences of those dramatic events continue to influence our complex mosaic of values and practices. Lawrence Hartmann's roots, his family, and his own career up through his presidency of APA mirror these developments and also shaped them.

Larry's father, Heinz Hartmann, was, of course, one of the most significant theoreticians in the entire history of psychoanalysis. His work on ego psychology was seminal in several senses. It brought forth a promising new phase of world psychiatry as well as psychoanalysis. It opened a pathway for research on ego psychology and adaptation that still remains to be plumbed from a biopsychosocial and/or a psychobiological perspective. Heinz Hartmann's move to the United States reflected the postwar emigration of Austro-German intellectuals

to this country. America became the world's center for psychoanalysis, and the impact of this development on America's psychiatry was momentous. Indeed, for a quarter of a century, American psychiatry was dominated by analytic theory and practice. Dora Hartmann, Larry's mother, was also a most distinguished psychoanalyst. Her prior career in pediatrics, before immersion into analysis, presaged Larry's capacities and motivation for child psychiatry, as did her love of games and sports, including mountaineering.

On both sides of his family, our President inherited and applied proclivities and capacities for a vigorous intellectual, artistic, athletic, and public life. A paternal great-grandfather was a leader in the Austrian revolution of 1848; he combined talents in poetry and prose with his political work. (Wouldn't it be nice if countries other than Czechoslovakia and the Ivory Coast facilitated leadership of this quality?) Replete with artists, physicians, historians, musicians, ambassadors, educators, naturalists, and many free spirits, Larry's family was cosmopolitan in the best sense of the word. It would be reductionistic, however, to formulate our President's life and career in simplistic continuity terms. Discontinuities, personal bents, and preferences have played a significant role. While influenced deeply by psychoanalysis—including a personal analysis—he has chosen a pathway that blends parental and family history into his own amalgam of interests in work and love. His companion, Brian Pfeiffer, with whom he has shared affection, intellectual interests, and travel for two decades, has also had a distinguished career in architectural history. Brian's special interest in philosophy, social criticism, and his energetic love of life complement Larry's style and scope. Ernest Hartmann, Larry's brother, demonstrates his own pattern of family continuity. Ernest is also a psychiatrist, and he is a psychoanalyst like his parents. He, too, however, has carved out his own career niche. Ernest Hartmann's commitments to research in the biology of sleep and dreaming have been creative and productive. More recently, Ernest's work on boundaries in the mind is redolent of Heinz Hartmann's contributions 50 years ago, but it is also different in method and concept. The brothers, Ernest and Larry, have different individual styles; Larry's interests are more clinical and educational, although he has mused occasionally in the past about converting his respect for new ideas and research into more of an investigative and theoretical career.

John Kennedy once had fun saying, at a Yale com-

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mencement where he was an honoree, that he now had the best of two possible worlds, a Harvard education and a Yale degree. Larry Hartmann has had the best of several worlds. His family moved from Vienna when he was one year old. They lived in Paris for a year, and Larry's first language was French, which he used and implemented in Geneva and Lausanne, prior to his move to New York when he was almost four. To be Larry Hartmann and to have grown up in Manhattan in the 1940s and early 1950s was a marvelous opportunity. The schools were first-rate, stimulating, and thorough. How nice to be a teacher and have a student who thrived in mathematics, English, sports, and the pleasure of learning.

Even before he matriculated at Harvard College, Larry's talents in literature, opera, and drama began to blossom. His love of classics has remained central to his life, up to the present. Recently, on a trip to Leningrad, Russian colleagues were surprised and very pleased to work with an American colleague so well steeped in their literary tradition. Once again, however, even in these passions there was discontinuity as well as continuity. Larry created his own mixture of classicism, personal history, and dry wit. At age 17 he wrote a spoof of Hamlet in which the prince was converted into the son of a Park Avenue psychoanalyst. Naturally, he starred in this drama. I wish I had seen it! At Harvard College, Larry immersed himself in history as well as literature. He served on the editorial board of the *Harvard Crimson* and was a drama critic, obviously preparing himself for a role in APA. In retrospect, it is not surprising that Larry was selected to be a Rhodes Scholar at Oxford, for work in English literature. What a marvelous opportunity to seep himself in college life, to walk, to make friends, and to be so close to the London drama scene. His admiration for Olivier, Gielgud, Richardson, and others was able to mature, and he continues that special interest today.

Fortunately for us, given the panoply of career choices, Larry opted to attend Harvard Medical School. He interned in pediatrics at the University of California at San Francisco and returned to Boston for psychiatric residency at the Massachusetts Mental Health Center. At that time, in the mid 1960s, the Center was a mecca for many gifted trainees. Its tradition was to produce first-rate educators, clinicians, and researchers with a commitment to public service. Humane Values and Biopsychosocial Integration could have been its credo also, but its special role in creating the dominant psychiatric ideological tenets of the 1960s was apparent to many; perhaps early in the next century another retrospective look at those values will help us reflect. The *Zeitgeist* of the Center, like the *Zeitgeist* of Manhattan at an earlier phase of Larry's life, influenced his adult development in a number of special ways. Commitment to social issues, broadly and specifically, and their place in psychiatry was very strong in teachers and leaders at the Center, and many students also became determined to change the shape of American psychiatry. Larry identified with these values but, as always, added his own

scope to them. Particular motivations affected his creation of a professional identity that included his electing a child fellowship at the Center; child psychiatry flourished at that time also, and its attraction was clearly overdetermined. That Larry chose to work in child psychiatry (albeit not exclusively) and then move toward a career pattern that emphasized private practice and teaching was a major personal choice given the broad array of career possibilities for him. He has had the knack of finding his own clear solutions amid much complexity and diversity, and he enjoys that process very much.

Fortunately for APA, Larry Hartmann also elected to become an active participant in Association affairs at an early age. Again, the overdetermination is manifest. From his families' involvement in sociopolitical history, his multicultural perspective on biopsychosocial processes, his passion for democracy, his stimulating milieu at the Massachusetts Mental Health Center, his wish to be active in the seeking of justice and equality for children, for women, for homosexuals, and for minorities, and his penchant for clarity and precision in finding balanced solutions—all of these forces played a role in his pathway toward leadership. Also playing a role was his passion for psychiatry as a field and his growing skill in the organizational processes necessary to advance the field. These skills are an interesting sidebar to our President. He has been, and still is, a parliamentary and constitutional student and painstakingly involved in facilitating order and precise use of language. In a way he has become a constitution-writing English teacher in psychiatrists' clothing.

Larry's ascending into the leadership of APA followed a career ladder that is becoming more of a paradigm these days. His involvement on the steering committee of the National Committee of Concerned Psychiatrists from 1971 to 1975 helped to catalyze his values and commitments, but he also worked his way up the ranks in APA and the American Academy of Child and Adolescent Psychiatry. The ladder included leadership roles in the Massachusetts Psychiatric Society, which soon evolved into his membership in our Assembly, where he served from 1976 to 1985. Occasionally, in the Assembly, Larry's image was like a patrician schoolteacher, but the respect for his underlying values steadily grew; so did his respect for others in the Assembly who expressed opinions contrary to his, as long as they did it fairly and clearly. Members of the Assembly, through the marvelously satirical voice of former Speaker Bill Sorum, once had fun making a caricature of Larry Hartmann. Would the Assembly elect a politically liberal, middle European prince as its Speaker? Yes, they did, and Larry loved being Speaker—and being a prince. Conscious of diverse policy opinions of the Assembly, he was eminently fair, but he also played a decisive role in leading the Assembly toward decisions that supported minorities, equitable distribution of power, and biopsychosocial integration. As Speaker, Larry began his long-term role in the APA Board of Trustees, where he has served since 1980. As Area I trustee, he mirrored New England's activism and sense

of social and economic justice but consistently applied his own brand of balance, order, humor, and, *mirabile dictu*, pertinent clinical vignettes. Good at APA politics, Larry followed his Area I electability with successive victories for the positions of Vice-President and President-Elect. Anyone knowledgeable about APA elections could note his shrewd assessment of how to win an APA election. The Prince could work the precincts, amass significant supporters, speak at numerous gatherings of voters, and turn out the vote.

Here, in his Presidential Address, you can read Larry's own enunciation of what he has tried to accomplish during his presidential year and what he hopes and aspires for psychiatry. Complex social, political, and economic pressures have certainly made all of us uncomfortable and test the limits of our adaptability. The forces of reductionism abound in manifest and subtle fashions. Many of our members long for the perceived halcyon days of the 1960s, and regressive tendencies also have a broad appeal. This past year has had more than its share of APA fiscal problems, highly publicized events that attacked or threatened our ethical fabric, international discontinuities and turmoil, ratcheting down of medical benefits, and concerns about recruitment into psychiatry. These and many other issues have preoccupied our 120th President. Nevertheless, he has had the energy, the foresight, and the commitment to see the forest as well as the trees. He has presided with his usual balance, wit, and precision.

He has traveled extensively, including involvement in

our Eastern European project last month. Larry Hartmann has had international interests and commitments superseding those of all but a few of our previous presidents. He has sought justice for psychiatric patients in South Africa, Chile, Saudi Arabia, and, of course, the former Soviet Union. In this enormous task, the interplay between the specific psychiatric issues and general questions of human rights have been clear in Larry's mind, his writing, and his actions. Somewhere, amid intergalactic space and sounds, I think I can hear bemused applause from Larry's great-grandfather and other members of his family. These interests, however, have been balanced and complemented by his concentration on domestic concerns involving our patients, our members, our allies, our minorities, and all of the major problems they encounter.

He has faced our problems squarely but pointed us to new solutions embodying his biopsychosocial principle and the humane values that must accompany the principle. In addition, he has had the capacity and the strength to support colleagues who experienced travail and loss during the year. As one of those who felt Larry's quiet support, understanding, and help, I can attest that our President's theme is a personal and living credo that I have learned to appreciate. Yes, Larry Hartmann is an extraordinarily cultured man, and we at APA have benefited greatly from the confluence of diverse historical, personal, and professional forces impinging on him so that he has chosen to and was elected to lead the American Psychiatric Association.

Revising Axis V for DSM-IV: A Review of Measures of Social Functioning

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***Objective:** Axis V, which uses the Global Assessment of Functioning Scale in the multiaxial system of DSM-III-R, is under review for DSM-IV. This article examines what is known about axis V and selectively reviews the literature on measures of social functioning to identify potential alternatives to the Global Assessment of Functioning Scale. **Method:** About 25 studies on the use, reliability, and validity of axis V in DSM-III and DSM-III-R are reviewed. In addition, nearly 30 measures of social functioning are reviewed and analyzed as potential substitutes for the Global Assessment of Functioning Scale. The analysis focuses on the strengths and weaknesses of each measure for assessing functioning on axis V. **Results:** Axis V measures are modestly reliable and valid but not widely used. The authors identify and discuss two particular limitations of the Global Assessment of Functioning Scale: 1) the combination of measures of symptoms and measures of social functioning on a single axis and 2) the exclusion of physical impairments from the rating of functioning. **Conclusions:** None of the measures of social functioning reviewed is clearly superior to the Global Assessment of Functioning Scale for use on axis V. A modified version of the Global Assessment of Functioning Scale, separating the measures of social and occupational functioning from the measures of symptoms and psychological functioning, is proposed for field testing, along with a new set of instructions permitting the rating of limitations due to both physical and mental impairments.*

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Axis V was introduced in *DSM-III* as a measure of "adaptive functioning" on a 7-point scale ranging from superior to grossly impaired. Axis V was modified

for *DSM-III-R* in an effort to increase its utility. According to *DSM-III-R*, axis V, the Global Assessment of Functioning Scale, is to be used to assess "psychological, social, and occupational functioning." It is "available for use in special clinical and research settings" (*DSM-III*). It is not a required element of patient evaluation and is regarded as a supplement to the "official" diagnoses (on axes I, II, and III). There is little evidence concerning how frequently axis V is used for planning treatment and predicting outcome (1).

As a result of the revision of axis V in *DSM-III-R*, a simple measure of adaptive functioning was replaced by a 90-point scale that combines assessments of psychological, social, and occupational functioning; it is based on the widely used Global Assessment Scale (GAS) (2). It was thought that the Global Assessment of Functioning Scale would be a more useful element of the multiaxial evaluation system than *DSM-III* axis V, because the GAS has been used in hundreds of studies and clini-

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cal settings. There is little or no information, however, on the impact of the changes made for *DSM-III-R* on the utility or acceptability of this supplementary axis.

This report reviews what is known about axis V of *DSM-III* and *DSM-III-R*, reviews other measures of social functioning, and discusses several options for proposed further revision of axis V for *DSM-IV*.

RELIABILITY AND VALIDITY OF AXIS V

A number of published studies have addressed the reliability or validity of *DSM-III* axis V.

Reliability

In the *DSM-III* field trials, the intraclass correlation coefficient (ICC) for axis V ratings of adult patients was 0.80 when the joint interview method was used and 0.69 for test-retest evaluations (3). Fernando et al. (4) reported a lower figure of 0.49 for the ratings of a multidisciplinary group of clinical workers on an inpatient service.

Russell et al. (5) found 64% agreement between raters of cases of child psychopathology who used a preliminary version of axis V consisting of a 4-point scale of current impairment in adaptive functioning. Using *DSM-III* axis V, Mezzich et al. (6) found an ICC of 0.61 for ratings of a mixed group of child and adolescent cases. Rey et al. (7) reported an ICC of 0.57 for a group of adolescents. All three of these studies had clinicians rate written case summaries rather than the patients in person.

Overall, reliability for axis V has been found to be higher than for axis IV. Given the relatively restricted diversity of clinicians, patients, information, and time frames in the published studies, however, the demonstrated reliability of axis V has not been especially good (8). Although special training in the use of the measures of functioning for axis V may improve reliability, we are not aware of any studies of the impact of training.

Validity

Most validity studies have compared adaptive functioning as measured by axis V for different patient groups identified by diagnosis or referral status. A few have approached concurrent or construct validity by comparing axis V ratings to other measures of adaptive functioning. The relation between axis V and disposition or treatment status has been studied, mostly retrospectively. Two studies have used prospective designs to examine the predictive validity of axis V.

Five studies have reported predictable diagnostic group differences on axis V in diverse patient populations. In a mixed group of inpatients and outpatients, Skodol et al. (9) found significant variation in axis V ratings across 10 diagnostic groups; patients with schizophrenia received the poorest ratings of adaptive

functioning, and patients with V codes, no axis I diagnosis, anxiety disorders, adjustment disorder, and major depression (single episode) received the best. In a sample of more than 10,000 patients, Mezzich et al. (10) found that depressed patients had higher axis V ratings than nondepressed patients. Trzepacz et al. (11) found that liver transplantation candidates who were delirious and who were seen by a consultation-liaison service had lower axis V ratings than nondelirious patients. Westermeyer (12) reported lower levels of adaptive functioning among Asian refugees to the United States who had any axis I diagnosis than among those who had none, and Fabrega et al. (13) found a trend toward greater impairment according to axis V at intake among patients whose axis I diagnoses were more complex. These investigators found a highly significant relation between complexity of axis I disorder and deficits in *current* functioning.

A sixth study, by Schrader et al. (1), had mixed results. These authors found no difference on axis V between psychotic and nonpsychotic, psychotic and organic, or nonpsychotic and organic patient groups. When psychotic patients were divided into those with affective psychoses and those with nonaffective psychoses, the former had higher levels of functioning than the latter, who also had lower levels than patients with nonpsychotic disorders. Bronheim et al. (14) reported that patients referred for psychiatric consultation from an otolaryngology service had better functioning on axis V than other referred patients.

Three studies have examined the relation of axis V to other measures. Skodol et al. (9) compared axis V to measures of social and occupational functioning included in the Psychiatric Epidemiology Research Interview (PERI) and other social network variables assessed independently. They found significant correlations between axis V adaptive functioning and both social and occupational variables, with occupational factors predominating. Westermeyer and Neider (15) found highly significant negative correlations between axis V ratings and two separate components of social networks—number of people and number of separate social groups—among patients with substance abuse. Finally, Rey et al. (7) reported that in their samples of adolescents, axis V functioned similarly to independent ratings of premorbid functioning and less like measures of social competence or present functioning.

In a series of analyses, Gordon and associates have examined the relation between axis V ratings and treatment status. Initially, Gordon et al. (16, 17) developed a measure called the "strain ratio," which is the ratio of axis IV ratings of severity of psychosocial stressors to axis V ratings, transformed in such a way that higher ratings indicate better adaptive functioning. They found that length of inpatient hospitalization was correlated with higher strain ratios: when patients' rescaled levels of functioning exceeded their scores on axis IV, they tended to remain in the hospital for a shorter period. Subsequently, Gordon and Gordon (18) reported predictable differences in axis V ratings between chroni-

cally ill state hospital patients, long-term inpatients, short-term inpatients, and outpatients.

Mezzich et al. (19) found that ratings of highest level of adaptive functioning in the past year correlated 0.27 with the decision to admit a patient for inpatient treatment from a walk-in clinic. These investigators found a greater correlation ($r=0.45$) between impairment in current adaptive functioning, measured over the preceding month, and inpatient disposition.

In the first of two prospective studies of the ability of axis V ratings to predict outcome, Mellsop et al. (20) found a significant relation between preadmission adaptive functioning as measured by axis V and symptomatic outcome at 6 months among inpatients. They also found, however, an even greater relation between outcome and functioning as measured by the self-report Social Adjustment Scale. In the second study of predictive validity, Beiser et al. (21) found that axis V was a powerful predictor of which patients who received a diagnosis of schizophreniform disorder early in a psychotic episode would, in fact, recover within the 6 months stipulated by *DSM-III* and which ones would not recover, necessitating a change in diagnosis to schizophrenia.

DSM-III-R Axis V

There are no currently published studies on the Global Assessment of Functioning Scale of *DSM-III-R*, but a number of the reports we have mentioned and two additional studies have some bearing on the changes in the adaptive functioning construct in *DSM-III-R*. The two major changes in concept are 1) the provision for rating both highest level of adaptive functioning in the past year and current functioning and 2) the inclusion of symptom severity, as well as indicators of social and occupational functioning, in the ratings.

With respect to the first change, Skodol et al. (9) found few differences between social and occupational functioning measured over the past year as compared to measured over the past month when these were correlated with axis V ratings of highest level of functioning in the past year. Rey et al. (7) also found a greater relation between axis V and independent ratings of pre-morbid, rather than present, functioning. The analyses of Fabrega et al. (13) and Mezzich et al. (6), however, point to the potential importance of current functional impairment as a consideration in diagnosis and treatment planning.

With respect to the second change, several different groups have attempted to divide axis V into its component parts and examine each component separately. In the study by Trzepacz et al. (11), separate ratings of current occupational, family, and social functioning all bore the same relation to delirious versus nondelirious diagnostic status as did the overall axis V rating. On the other hand, Mellsop et al. (20) observed some variations in the relation between three similar factors and outcome prediction and suspected that global ratings of adaptive functioning masked significant variability.

Beiser et al. (21) believed that the inclusion of symptoms in *DSM-III-R* axis V would undermine its ability to discriminate schizophreniform from schizophrenic patients. Gordon et al. (22) showed that symptom improvement and functional improvement, as measured by axis V, did not go hand in hand in discharged patients followed in outpatient treatment over time. And finally, Skodol et al. (23) demonstrated that symptoms had a larger effect on axis V ratings, in terms of explained variance, than adaptive functioning variables and tended to detract from the latter's significance. Although the effect of symptom measures on explained variance may be taken as support for changing axis V into the Global Assessment of Functioning Scale, the change also may make axis V more redundant with axis I diagnoses. If a major objective of a multiaxial approach is the quasi-independent assessment of different domains relevant to a comprehensive psychiatric diagnosis, then explicit inclusion of symptoms in the axis V ratings would seem to defeat this purpose.

STRENGTHS AND WEAKNESSES OF AXIS V

This review suggests that axis V is a reasonably valid measure of adaptive functioning, limited in part by its modest reliability. In addition, some problems have been identified with the changes introduced at the time of the revision of *DSM-III*. For example, there is mixed evidence on the value of obtaining measures of functioning during two time periods (i.e., past month and past year). (As might be expected, the value seems to depend on the nature of the question being asked, suggesting that assessments in both time periods have merit. Consequently, there is no great pressure to change axis V, again, to a rating of a single period.) Two other problems, however, are believed by some to limit the utility of axis V in *DSM-III-R*. In particular, there is concern that 1) the assessment of functioning is attributed to mental impairment alone and 2) one axis combines measures of psychological, social, and occupational functioning. In the first instance, it may be impossible to disentangle the combined limitations imposed by mental and physical impairments; in the latter, it may be too difficult to assess these distinct domains of functioning with a global measure.

These problems may be related. The progenitor of the Global Assessment of Functioning Scale, the GAS, was designed as a global measure of psychopathology, focusing heavily on current psychological functioning. As such, it was logical to focus on functioning related to mental disorders alone. When the global GAS approach is used more broadly, emphasizing social and occupational functioning over the past year, it may be much more problematic to attribute functioning to a mental disorder alone. Furthermore, when the GAS model is used in general medical settings or with elderly patients who have multiple impairments, it is even more difficult to make such attribution reliably (personal communication, E. Caine).

The combination on a single axis of measures of psychological, occupational, and social functioning is problematic for two reasons: 1) it violates the principle of a multiaxial system in which each axis "refers to a different class of information" (*DSM-III-R*), and 2) it may also confuse raters because of the complexity of making a single rating which integrates three different dimensions that do not always vary together. As we have noted, there is evidence from Skodol et al. (9, 23), supported by the findings of other studies (20–22), that ratings on axis V are highly correlated with those on axis I, indicating that axis V does not provide a sufficiently independent class of information. In addition, other investigators (24–27) have indicated that psychological functioning often does not correlate well with social and occupational functioning. Although a recent set of studies by Liberman (28) suggest a significant relation between symptom measures and occupational functioning, it is a relationship mediated by functional impairments in the capacity to work (such as limitations in social interaction and activities of daily living).

Before deciding to recommend retaining the Global Assessment of Functioning Scale for axis V or changing to another measure, we turned again to the literature.

MEASURES OF SOCIAL FUNCTIONING

We reviewed the literature on measures of social functioning in an effort to find out what other measures might be used as models for axis V. Our review relied heavily on two articles: "The Assessment of Social Adjustment: An Update" by Weissman et al. (29) and "Functional Assessment in Rehabilitation" by Wallace (30). Promising instruments were viewed in more detail from their original sources. Although we reviewed each of the instruments for depth and breadth of measures, appropriate target population, and psychometric properties, the special criteria we used to evaluate these scales for possible inclusion in axis V focused also on simplicity ("user friendliness") and unidimensionality (i.e., involving a single class of information). The instruments reviewed in the articles by Weissman et al. and Wallace are shown in table 1; citations of the original references are provided. The reviews of each of these instruments are summarized in table 1 along several dimensions, including psychometric properties and method of scoring. Each instrument is placed into one of seven groups on the basis of inclusion of symptoms in the instrument or schedule, depth and breadth of dimensions of functioning, and applicability to the general population (rather than to a specific clinical group).

As shown in table 1, group 1 consists of the Denver Community Mental Health Questionnaire and the KDS-15 Marital Questionnaire, which include symptom measures, do not include role performance measures (especially the Denver Community Mental Health Questionnaire), and focus on specific clinical groups (i.e., community mental health clinic clients and married couples). Group 2 includes the Katz Adjustment

Scale, Personal Adjustment and Role Skills Scale, Psychiatric Status Schedule, Psychiatric Evaluation Form, and Current and Past Psychopathology Scales. This group also includes symptoms, is somewhat more inclusive of areas of functioning than group 1, and is broadly applicable to the entire clinical population. It is similar to group 5, which includes the Social Behaviour Assessment Schedule and the Self-Assessment Guide, both of which are more detailed measures of functioning than the instruments in group 2. Group 3 includes the Rehabilitation Evaluation of Hall and Baker and the Community Living Assessment Scale, which do not include symptom measures, which focus on a narrow domain of functioning, and which principally apply to a limited population in 24-hour care. The Personal Resources Inventory and Interview Schedule for Social Interaction are in group 4; they do not include symptom measures, and they focus on a narrow range of functioning but are more broadly applicable than the instruments in group 3.

Groups 6 and 7 are similar. All of the instruments (Community Adaptation Schedule, Structured and Scaled Interview to Assess Maladjustment, Standardized Interview to Assess Social Maladjustment, Community Adjustment Profile System, Social Stress and Functioning Inventory for Psychotic Disorders, Social Functioning Schedule, and the various versions of the Social Adjustment Scale) measure a broad range of functioning without assessing symptoms. The social functioning scales from the PERI (27) and the Longitudinal Interval Follow-up Evaluation (56) were not included in either review and should be added to category 7. The same is true for the Role Activity Performance Scale (57). All are applicable to a broad population, and almost all give global ratings, but the Community Adaptation Schedule is judged by Wallace (30) to have limited information on its psychometric properties.

We refer the interested reader to the two review articles and the original material in the literature for a more comprehensive assessment of these instruments. Our brief review focuses on the suitability of alternatives to the Global Assessment of Functioning Scale for inclusion in *DSM-IV*.

Given our criteria of unidimensionality, the instruments in groups 3, 4, 6, and 7 should be considered as alternatives to the Global Assessment of Functioning Scale. Groups 3 and 4, however, cover too limited a domain of functioning, and group 4 is also limited in its applicability. The Community Adaptation Schedule (group 6) also might be eliminated because of limited psychometric data, leaving the instruments in group 7. If the criterion of unidimensionality is deemphasized, then groups 1, 2, and 5 also must be considered. Group 1 is a weaker choice because of limitations in range of functioning measured and applicability, as well as lack of a global measure. Groups 2 and 5 include many meritorious measures of symptoms and functioning. In fact, the GAS, the basis for the Global Assessment of Functioning Scale, is derived from the work of some of the same investigators who developed the instruments in group 2.

In terms of user friendliness, global ratings are given by instruments in groups 2, 3, 6, and 7. All of these ratings, however, are based on fairly extensive interview schedules or structured self-reports. In part, their structured formats make them reliable and recommend them for use in research. On the other hand, none of these measures could be regarded as simple enough for routine use in clinical practice.

OPTIONS

The approach to change for *DSM-IV* has been characterized as "conservative," requiring compelling arguments and extensive documentation to support alterations in the nosology (58). Although our review suggests a number of problems with the current Global Assessment of Functioning Scale, there are problems with all of the potential alternatives as well. Before considering a complete change in axis V, there should be evidence of severe problems with the Global Assessment of Functioning Scale and/or an outstanding new alternative. Considerable experience with the Global Assessment of Functioning Scale (and its predecessor, the GAS) and its apparent simplicity made it a choice for *DSM-III-R* and argue for its retention—with some significant modification. As we have noted, the principal limitations of the Global Assessment of Functioning Scale are 1) the combination of ratings of symptoms and functioning on a single scale and 2) the rating of functioning based on mental impairment alone rather than the combined effect of mental and physical impairments.

The Global Assessment of Functioning Scale could be modified to separate the rating of symptoms and psychological functioning from the rating of social and occupational functioning. We propose a field test of a modification of the current axis V scale. (See appendix 1 for an example of one modification.) We have divided the current Global Assessment of Functioning Scale into two separate scales, one to measure global symptomatology and psychological functioning, the other to measure social and occupational functioning. The modified scale in appendix 1 retains the same scale points and many of the anchoring descriptors that are used in the current Global Assessment of Functioning Scale. We hypothesize that this change will reduce confusion and improve the independence of the ratings of these domains. This hypothesis, as well as the reliability of the measures, should be assessed in a field trial of the modified scale. The results of the field trial may indicate a need for more elaborate anchoring descriptors, which could then be developed. If it is found that the modified Global Assessment of Functioning Scale shown in appendix 1 is more reliable, produces ratings on social and occupational functioning that are significantly more independent of axis I than the current scale ratings, and is more acceptable to clinicians who use it in the field trial, then the modified scale should be used as a substitute for the current scale.

TABLE 1. Measures of Social Adjustment and Functioning

Instrument	Inclusion of Symptoms
Group 1	Yes
Denver Community Mental Health Questionnaire (DCMHQ) (31, 32)	
KDS-15 Marital Questionnaire (KDS-15) (33)	
Group 2	Yes
Katz Adjustment Scale (KAS) (34)	
Personal Adjustment and Role Skills Scale (PARS) (35)	
Psychiatric Status Schedule (PSS) (36)	
Psychiatric Evaluation Form (PEF) (37)	
Current and Past Psychopathology Scales (CAPPS) (38)	
Group 3	No
Rehabilitation Evaluation of Hall and Baker (REHAB) (39)	
Community Living Assessment Scale (CLAS) (40)	
Group 4	No
Personal Resources Inventory (PRI) (41)	
Interview Schedule for Social Interaction (ISSI) (42, 43)	
Group 5	Yes
Social Behaviour Assessment Schedule (SBAS) (44)	
Self-Assessment Guide (SAG) (45)	
Group 6	No
Community Adaptation Schedule (CAS) (46)	
Group 7	No (except SSIAM)
Structured and Scaled Interview to Assess Maladjustment (SSIAM) (47, 48)	
Standardized Interview to Assess Social Maladjustment (SIASM) (49, 50)	
Community Adjustment Profile System (CAPS) (51)	
Social Stress and Functioning Inventory for Psychotic Disorders (SSFIPD) (52)	
Social Functioning Schedule (53)	
Social Adjustment Scale (SAS); Self-Report (SAS-SR); Version II (SAS-II) (54, 55)	

The modified scale's measure of social and occupational functioning is similar conceptually to the original *DSM-III* axis V measure of adaptive functioning. The modified scale's measure of global symptomatology and psychological functioning would be a new assessment. It might be included as a second rating on axis V or rated on a separate axis. It is likely that ratings on this measure will be highly correlated with axis I. To some extent it also may be redundant with the proposed

TABLE 1 (continued)

Depth	Scoring	Applicability	Psychometric Characteristics	Other Characteristics
Not much depth	Give specific and more general scores	Highly specific	Reliable and valid	
Little attention to role performance		Designed only for mental patients		
Looks only at marriage		Designed only for married couples		
Not much depth	Give specific and more general scores	Generally applicable	Reliable and valid	
Ignores many roles; does not discuss cause of problems				Short and simple; can be used with significant other
	Gives global rating			
Does not discuss cause of problems	Gives global rating			Flexible; includes probes; can be used with significant other
Does not discuss cause of problems	Gives global rating			
Does not discuss cause of problems	Gives global rating			
Not much depth	Give specific and more general scores	Highly specific	Reliable and valid	
		Designed only for institutionalized patients		Well explained; simple to use; easy to interpret
	Gives global rating	Designed for individuals in residential care facility	Should be further investigated	
Not much detail; look only at individual's support network	Give specific and more general scores	Generally applicable	Reliable and valid	
			Should be further investigated	
Very detailed	Give specific and more general scores	Generally applicable	Reliable and valid	
				Self-report; short
Very detailed	Gives specific and more general scores; also gives a global rating	Generally applicable	Reliability and validity need further investigation	Self-report
Very detailed	Give specific and more general scores	Generally applicable	Reliable and valid	
				Careful about interviewer bias; can be used with significant other
	Gives a global rating			Can be used with significant other
				For significant other
				Can be used with significant other
	Gives a global rating			Flexible; can be given to significant other; self-report available; good with psychotic patients

inclusion of severity ratings for each mental disorder (personal communication, J. Mezzich).

The instruments in group 7 should be examined further as potential substitutes in the future, especially if there are problems with the Global Assessment of Functioning Scale or its modification. If warranted by further examination, there should be a field trial of the best global measure or measures from group 7 for use in general clinical practice *without* a standardized schedule.

A simple modification in the instructions for rating the Global Assessment of Functioning Scale could address the other identified problem with axis V. As we have noted, when assessing certain patients, it is difficult (or impossible) to separate the effects of mental impairments from physical impairments contributing to limitations in social and occupational functioning. Axis V in *DSM-III* did not instruct the rater to make any such distinction. In contrast, the instructions for the Global Assessment of Functioning

Scale explicitly call for a rating of limitations of functioning due to mental impairments alone. We propose a field test of a modification of the instructions for the modified Global Assessment of Functioning Scale (Functioning) to assess social and occupational functioning due to the *combined* effects of mental and nonmental medical impairments (appendix 1).

CONCLUSIONS

The options under consideration by the Work Group on Multiaxial Issues include some combination of changes in the basic structure of the Global Assessment of Functioning Scale and in the instructions. Our review of the relevant literature suggests both of these potential modifications, following a conservative strategy for change. The final decision should be based on a field test of these recommendations. It is our hope that these modest changes will increase the utility and use of axis V.

In following a less conservative strategy for change, several other avenues of research and scale development are indicated. First, there is a need to study the impact of various approaches to training on the reliability of measures of social and occupational functioning. Second, our review suggests the need for different measures for different areas of functioning. The conservative strategy and requirement for simplicity, applicable to multiaxial diagnosis and DSM, may be overly limiting for valid and useful measurements of functioning. A more multidimensional approach to measuring social and occupational functioning in individuals with mental disorders may be superior. The research literature suggests numerous more complex measures. Further investigation may produce simpler measures of each of the multiple dimensions of functioning that could be used in practice as well as research.

Leaders in general medicine have called for the use of simple measures of functioning in routine clinical practice—to support the need for measures of clinical outcome (59–61). Feinstein et al. (62) warned of the problems associated with these needed measures, noting that the measures should be “sensible” as well as reliable and valid. The current Medical Outcomes Study (61) has been using a “short form” measure of several dimensions of functioning and health status (63) and has adapted it for use in assessing outcomes in a variety of clinical conditions, including depression (64, 65). The field of psychiatry has growing experience with functional assessment and the measurement of medical outcomes. We have the opportunity to be in the forefront of this important area of health care research and practice.

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APPENDIX 1. Modification of the Global Assessment of Functioning Scale: Mental and Physical Impairments Functioning Scale (GAFS-M)

Consider social and occupational functioning on a hypothetical continuum of mental health-illness. Include impairment in functioning due to physical limitations as well as mental impairments. Use HIGHEST LEVEL OF FUNCTIONING IN PAST YEAR (i.e., highest level of functioning for at least a few months during the past year).

Code

- | | |
|----|---|
| 90 | Good functioning in all areas, interested and involved in a wide range of activities, socially effective |
| 81 | |
| 80 | No more than slight impairment in social and occupational functioning (e.g., missing a few deadlines or appointments) or school functioning (e.g., temporarily falling behind in school work) |
| 71 | |

70	Some difficulty in social or occupational functioning (e.g., frequent work absences, work occasionally incomplete or judged "not up to standards") or school functioning (e.g., occasional truancy, or theft within the household) but generally functioning pretty well; has some meaningful interpersonal relationships	40	Major impairment in several areas, such as work or school, family relations, judgment (e.g., avoids friends, neglects family, is unable to work; child frequently beats up younger children, is failing at school)
61		31	
60	Moderate difficulty in social, occupational, or school functioning (e.g., few friends, conflicts with co-workers, unable to complete work assignments, unsatisfactory work performance)	30	Inability to function in almost all areas (e.g., stays in bed all day; no job, home, or friends)
51		21	
50	Serious impairment in social, occupational, or school functioning (e.g., no friends, unable to keep a job at expected or prior level of performance)	20	Occasionally fails to maintain minimal personal hygiene (e.g., smears feces); unable to function independently
41		11	
		10	Persistent inability to maintain minimal personal hygiene; unable to function without harming self or others or without considerable external support (e.g., nursing care and supervision)
		01	

Judicial and Legislative Responses to Cost Containment

Lloyd I. Sederer, M.D.

Cost containment through reduction of insurance benefits and aggressive utilization review is increasingly risking the sacrifice of good clinical care in the pursuit of financial objectives. This article provides examples of judicial and legislative responses to perceived fiscal intrusions into clinical practice. Principles for asserting clinical goals in the cost containment process are also provided to assist in the inevitable negotiations and battles ahead.

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The cost of health care in the United States is now perennially exceeding the growth of the national economy. Furthermore, vast numbers of American citizens (estimates are 34-37 million people) have no access to health care insurance benefits, and tens of millions more are underinsured. Finally, there is no national or overarching health care policy to shape the future nature of this health care system (1-6). As a consequence, a variety of measures have been undertaken as ostensible solutions to this highly problematic triad of circumstances.

For clinicians, patients, and families, the most disturbing "solutions" have been efforts to reduce health care costs, especially psychiatric and substance abuse costs, by constricting insurance benefits and by aggressive utilization review. Effective utilization review can protect patients from unnecessary care and can allow for flexible use of benefits. However, an explosively growing industry of managed care organizations coupled with limited and potentially decreasing insurance benefits threatens to sacrifice patient care on the altar of presumed fiscal responsibility (7, 8).

This article provides illustrative and important (but by no means exhaustive) examples of the judicial and legislative initiatives that have attempted to reassert clinical priorities in the cost containment process. The

cases and laws summarized here, some involving psychiatry and some involving general medicine, are guideposts as we try to maintain standards of professional practice in this era of cost containment.

UTILIZATION REVIEW

Utilization review is the process of determining whether medical care is needed and at what level of intensity (e.g., inpatient versus outpatient, surgical versus medicinal) (9). Utilization review is a primary activity of managed care organizations, principally through prior approval and concurrent review.

Judicial Cases

Utilization review practices of third-party insurance companies and fourth-party managed care organizations have been challenged in the courts since the 1970s. In the court cases summarized here, the conflict between clinicians and proponents of cost containment is well illustrated.

Wickline v. State of California (10) is regarded as a landmark case in utilization review, although it did not involve psychiatric illness. Lois Wickline was covered by Medi-Cal (Medicaid of California). In 1976 she received utilization review approval for admission to a California hospital for surgical treatment of obstruction of the terminal aorta (Leriche's syndrome). On the day of her surgery, she had to undergo a second operation for a blood clot that had formed in the graft. Five days later she underwent lumbar sympathectomy for

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pain symptoms secondary to vessel spasm. Because her insurance approval was to expire 4 days later, her doctors asked for an 8-day extension. The utilization review organization approved 4 days, which her physicians did not appeal. She was discharged after the 4-day extension. Nine days later Mrs. Wickline required emergency readmission for an infection and clotting at the site of the graft. She went on to require below-the-knee amputation of her right leg, and when healing did not proceed, she had to undergo above-the-knee amputation.

Mrs. Wickline, instead of seeking damages from her doctors, sued the State of California and its medical review organization. In trial court she was awarded \$500,000. In appellate court the state was not regarded as negligent, and the lower court's decision was reversed. The Supreme Court of California declined to review the case, thereby rendering the appellate court's decision final.

Two critical lessons emerge from the *Wickline* case. The first is that medically inappropriate decisions which derive from cost containment practices can be torts. The court stated that a "patient who is harmed when care which should have been provided is not provided should recover from all responsible for deprivation of care, including, when appropriate, a health care payer." The court added, "Third party payers of health care services can be held legally accountable when medically inappropriate decisions result from defects in designs or implementation of cost containment mechanisms." However, there is a second crucial lesson, which is best articulated by also quoting the court: "A physician who complies without protest . . . when his medical judgment dictates otherwise, cannot avoid his ultimate responsibility for his patient's care." In effect, the *Wickline* case broke ground by holding the insurer liable, but only if the physician has fully pursued all the appeals processes available to him or her. This is clearly a practice guideline for physicians rendering care and encountering denial of insurance coverage.

Hughes v. Blue Cross of Northern California (11) was upheld in appellate court in 1988 and held Blue Cross of Northern California responsible for \$150,000 in compensatory damages and \$700,000 in punitive damages. The court found that Blue Cross was engaged in egregious utilization review practices: only fragments of important records were obtained; there appeared to be only a cursory review of the records; the reviewing consultant disclaimed any obligation to pursue diligently the materials on the case; and there were uninformative follow-up letters to the physicians involved regarding the denial of benefits. Hughes was a 21-year-old, seriously psychiatrically ill man whose history began in 1981 with a hospitalization after a drug overdose and self-inflicted stab wounds to the abdomen with a screwdriver. The patient had multiple hospitalizations over the course of a year and had a deteriorating course. Portions of two hospitalizations were subsequently denied coverage by Blue Cross, without their having obtained adequate records and without their explaining the medical grounds for the denial. The court decided

that the insurer acted in bad faith by behaving with "conscious disregard of the insured's rights." It was this breach of the covenant of good faith and fair dealing that resulted in the heavy punitive damages. Clinicians, patients, and families can and should expect careful and diligent utilization review by payers.

Insurers, however, are not bound to follow strictly the clinical opinion and treatment plan of the attending physician (12). This creates a sometimes useful exchange of clinical ideas but places the patient in the position of having to pay for what is usually prohibitively expensive treatment (e.g., hospitalization) if his or her doctor loses the debate with the utilization reviewer. Timely review processes, required by contract or law, would help to minimize this frequent problem.

Wilson v. Blue Cross of Southern California (13) is a case of particular importance to practicing psychiatrists, because it is recent and it involves the death of a patient discharged because insurance coverage was denied. In 1983 Howard Wilson was admitted to a Los Angeles hospital with diagnoses of major depression, drug dependence, and weight loss. His admitting physician recommended 3-4 weeks of hospital care. Wilson was discharged 10 days after admission, when his insurer denied benefits and the patient and family had no money to support further inpatient treatment. Three weeks later Mr. Wilson took his life by overdose. His parents subsequently sued Blue Cross of Southern California and their review organization, Western Medical Review. The case had a summary judgment of dismissal in Superior Court in Los Angeles. On appeal, the court held that the contractor (namely, the insurer) could be at least partially "liable if negligent conduct was a substantial factor in bringing about the suicide." The appellate court reversed the lower court and remanded the case back to trial court, where it must be retried. This case may be another crucial precedent in holding managed care organizations liable for adverse outcomes secondary to denial of insurance benefits.

Varol v. Blue Cross/Blue Shield (14), concluded in 1989, is an important warning to physicians contracting under managed care plans. Although the court held that this case could not go forward because of an ERISA preemption (the Employment Retirement Income Security Act places certain insured organizations under federal rather than state statute), the court used the occasion to speak firmly to physicians. In this case a group of psychiatrists providing care under a Blue Cross/Blue Shield managed care contract for General Motors alleged that their contract impinged on the proper treatment of patients. The court retorted that a contract is binding and must be either terminated or honored, not altered by the court. To quote the court: "How can doctors challenge the provisions to which they agreed? . . . challenge only the provisions they do not like? . . . ask the court to modify the contract to their liking?" Furthermore, "plaintiffs are saying in effect, 'since I am weak in my resolve to afford proper treatment, the Blue Cross/Blue Shield preauthorization program would induce me to breach my ethical and legal duties . . . The

court must protect me from my own weakness' " (14, p. 833). Clearly, the court ruled that doctors are to be held to their contractual arrangements.

Finally, a case recently decided in a U.S. District Court, *Nazay v. L. Miller/Bethlehem Steel* (15), challenged the legality of prior approval, which is crucial to virtually all types of managed care. Nazay was a retired employee who was held responsible by an insurer for 30% of the costs of his hospital care for heart disease because he had neglected to obtain prior approval. Because his care was regarded as medically necessary, the court regarded the penalty as "arbitrary and capricious." The case is now under appeal. If the decision is upheld, a precedent would be established that would outlaw prior approval of medically necessary care by managed care plans.

Legislation

At the time of this writing, 19 states have enacted some type of utilization review legislation. Maryland was the first to enact such legislation; the states that have followed are Arizona, Connecticut, Florida, Georgia, Hawaii, Kentucky, Maine, Minnesota, Mississippi, Missouri, Montana, North Carolina, North Dakota, Oklahoma, Pennsylvania, South Carolina, Texas, and Virginia.

Many common provisions exist among these state laws. Articulated appeals processes, accessibility of reviewers to doctors and patients, clinically trained reviewers, and confidentiality of records tend to be basic regulatory requirements. Open and available review criteria and a requirement that only a physician can render an insurance denial are standards that have been established in some states (e.g., Connecticut, Missouri, and North Dakota have the standard for open review criteria, and Hawaii, Texas, and Montana have the standard of denial by a physician only).

Many other states are considering legislation to regulate the practices of managed care organizations and insurers providing utilization review. Utilization review companies continue to oppose these legislative initiatives and instead offer voluntary self-regulation through a nationally based accreditation association (16). In one form or another, it appears likely that utilization review will be increasingly standardized and regulated in the years to come.

INSURANCE BENEFITS

Cost containment has also been pursued by reducing the insured population's benefits. Patients, families, and professionals in turn have sought judicial and legislative remedies for perceived injustices.

Judicial Cases

Benefits for psychiatric disorders and substance abuse generally have been differentiated from benefits

for medical/surgical disorders, with less coverage being the rule (e.g., fewer covered days and dollars, higher copayments and deductibles). Several court cases have challenged this unfavorable and stigmatizing differentiation, particularly for the severely mentally ill.

Arkansas Blue Cross/Blue Shield v. Doe (17) was upheld in appellate court in 1987. In this case, a man whose daughter, a minor, had bipolar disorder sued Blue Cross/Blue Shield for the benefits that he had not obtained because of the limit on benefits under the mental health provisions of his policy. The principal argument in the case was that bipolar disorder is a biological disorder, and therefore the benefits should be on a par with those received for any other physical condition. The Arkansas court held that, indeed, bipolar disorder is a physical condition and that the insured was entitled to the benefits for a physical, not a mental, disorder. A case brought by the father of a patient against the Mutual Insurance Company of New York and B'nai B'rith (the *Rosenthal* case) is similar to the Arkansas case and was settled in late 1990 out of court (18).

Kunin v. Benefit Trust Life Insurance Co. (19) was a case in which a father brought action to recover benefits for the treatment of his autistic son at UCLA Neuropsychiatric Institute. The boy was admitted in 1986 for 30 days, and \$55,000 in hospital charges accumulated. The psychiatric benefits were limited to \$10,000. The father alleged that autism is a biological disorder. The court held that autism should be covered under medical, not mental, benefits and ordered payment by the insurer. The *Doe*, *Rosenthal*, and *Kunin* decisions are important precedents in a growing effort to establish parity of psychiatric and medical benefits.

Doe v. Guardian Life Insurance Co. et al. (20) was a class action suit brought by the Chicago National Depressive and Manic-Depressive Association in Cook County Circuit Court against two of the largest insurance corporations operating in Illinois, Guardian Life and Travelers' Insurance. The association alleged that manic-depressive illness is a "physical or biological illness," and, consequently, payments for the treatment of this mental illness should be equal to those for physical or biological illnesses. This case was dismissed by the court because of a technical problem, namely, that the court regarded the National Depressive and Manic-Depressive Association as "lacking any standing to sue under ERISA." The substance of the case was never addressed. Nevertheless, this was yet another effort to seek nondiscriminatory benefits for major mental illnesses.

Another case that failed in court is that of *Teti v. US Healthcare* (21). US Healthcare is a large managed care organization with significant activity in Pennsylvania, where this case was filed under the Racketeer Influenced Corrupt Organization Act. Awards under this act include treble damages and lawyers' fees. The plaintiff alleged that US Healthcare engaged in fraudulent behavior by misrepresenting its services (false advertising), because it failed to disclose financial compensation arrangements with physicians and the available specialty and hospital services. The plaintiff argued that

these arrangements discouraged the provision of services and that, consequently, consumers could not realize the benefits they had purchased. This case was dismissed by the court in December 1989.

Finally, the potential for a managed care organization to reduce union-negotiated health benefits was alleged in a class action suit against the state of Ohio (22, and personal communications from the Ohio District Branch of APA). The state of Ohio, which has 50,000 employees, had contracted for American Biodyne to manage its mental health and substance abuse benefits, anticipating that this would save \$4.5 million. The plaintiffs alleged that the service plan devised by American Biodyne would not correspond to the benefits that had been worked out in collective bargaining. In addition, there were many concerns among clinicians that American Biodyne's method of conducting its utilization review would be intrusive and would interfere with patients' access to care. Litigation was dropped because of the high costs of pursuing the case and because of the anticipated difficulties in proving that "intrusive case review" reduced the union-negotiated benefits package. The *Teti* case and the class action suit against Ohio failed to limit, through case law, the financial, referral, and utilization practices of managed care organizations.

Legislation

In a recessionary economy and in a time of belt tightening, it is sometimes an achievement to retain benefits. It has been especially heartening, therefore, to see expansion of benefits, which has occurred in two entitlement programs.

A remarkable coalition of interest groups came together in 1990 to bring about the progressive expansion of Medicaid benefits to all poor children. By the year 2001, all children who are eligible for Medicaid will be covered to the age of 18 (23). The federal government, the Health Insurance Association of America (representing the insurers), the National Association of Children's Hospitals, the National Association of Manufacturers, the American Medical Association, the Americans for Democratic Action, the American Hospital Association, the American Academy of Pediatrics, and Blue Cross/Blue Shield fashioned an alliance to bring this legislative effort to fruition. Perhaps this broad alliance of interest groups will have an opportunity to help legislate a national health insurance policy for all adults after the 1992 national election.

The second example of expansion of benefits, affecting psychiatry, involved the expansion of Medicare ambulatory care benefits from \$500 initially to \$1,100, then to \$2,200, and then, finally, to elimination of any benefit cap. This has been the only recent expansion of any type of Medicare benefit. Increased understanding of the biological bases of certain mental illnesses and reduction of stigma were instrumental in APA's achieving these gains.

Important legislative initiatives for insurance cover-

age for mental illness which is equal to that for medical/surgical disorders are also underway. Three states—Texas, Maine, and Maryland—have passed laws requiring that "biologically based" mental disorders have parity coverage. Although the states vary in their designations of the disorders to which the laws apply, all three include schizophrenia, major depression, and bipolar disorder. In 1989 California passed a nondiscriminatory coverage bill for five mental disorders, but this has not been implemented. In California a universal access bill, recently filed, does incorporate parity coverage for severe mental disorders (24, and minutes of the June 8–10, 1991, meeting of the APA Joint Commission on Government Relations). Other states and mental health advocacy organizations may want to pursue such groundbreaking parity legislation.

DISCUSSION

Faced with a recessionary economy and global competitive concerns, business and government in this country have no choice but to seek expense reductions. Health care has been particularly vulnerable to such reductions because of its robust growth and historical tendency (culturally supported) to do as much as possible. The economic shibboleth of the latest cost containment efforts in this country is managed care. An industry that promises to reduce costs has erupted. However, insurers and managed care organizations do not work for patients, and they do not work for families. These companies are employed by business and government to administer and manage health care benefits. In contracts in which strict budgetary controls apply (such as managed care), the insurer/managed care organization must contain costs or it will either lose its contract or suffer financial loss. As a consequence, these companies are inherently in conflict with doctors and hospitals who operate under a traditional medical ethic in which their primary responsibility is to the patient (not the dollars).

The utilization review litigation and legislation reviewed in this article highlight this conflict. Patients, families, and clinical care providers have gone to court to protect their interests. Legislative initiatives have sought to create responsible practices for utilization review organizations. Unless cost control is checked by litigation and regulation, it is likely to compromise patient care.

The benefits litigation and legislation reviewed in this article have sought to protect patients and families from discriminatory practices. Unless benefits for psychiatric and substance abuse disorders are properly recognized as essential and on a par with general medical benefits, the care of patients with these disorders will be undermined and progressively diminished.

The battle between costs and care is not new. Recent fiscal and political pressures, however, have intensified and will intensify this battle. As clinicians, we have principles that we can use to guide us in the years to

come. These principles apply in our professional practice, in court actions, and in legislative endeavors.

Fundamental to these principles is the recognition that cost containment cannot be at the expense of patients and, consequently, that responsible managed care must primarily attend to clinical decision making, not fiscal decision making. Open, professionally developed standards of utilization review (practice guidelines), rendered by credentialed professionals, must replace proprietary, secretive decision making. And no professional reviewer should receive incentives to deny care. Liability for adverse clinical outcomes secondary to negligent utilization review practices must continue to be aggressively sought by patients and families. Psychiatric and substance abuse benefits must be protected from elimination as employers seek low-cost policies (25, 26). Moreover, these benefits, especially for the severely mentally ill, should have parity in days, dollars, and deductibles with general medical and surgical benefits. Finally, every effort must be made to educate patients, families, employers, and government about mental illness and its true costs, especially if it is not covered and not treated. It is only by further destigmatizing mental illness and by demonstrating the efficacy of available treatments that mental health professionals will acquire the allies necessary to emerge successfully from the battles ahead.

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Association of β -Endorphin With Specific Clinical Symptoms of Depression

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***Objective:** Abnormalities in plasma concentrations of β -endorphin-like immunoreactivity (β -endorphin) have been reported in depressed patients. This study was done to test the hypothesis that specific clinical characteristics of depression are associated with plasma β -endorphin concentration. **Method:** Plasma β -endorphin was evaluated in 20 depressed patients diagnosed according to DSM-III-R and in 23 age- and sex-matched comparison subjects, and each was evaluated with the structured Schedule for Affective Disorders and Schizophrenia (SADS). Twelve SADS items involving dysphoric mood and related symptoms were chosen for analysis. **Results:** Within the group of all 43 subjects and within the depressed group, β -endorphin level correlated significantly with psychic anxiety and with phobia. In the depressed group only, β -endorphin also correlated significantly with obsessions/compulsions. Concentration of β -endorphin was not significantly correlated with score on the Hamilton Rating Scale for Depression or Beck Depression Inventory or with scores on other SADS symptom items, including somatic anxiety, insomnia, subjective anger, overt anger, agitation, psychomotor retardation, panic attacks, appetite loss, or total weight loss. In the group of 23 comparison subjects, β -endorphin did not correlate with Beck or Hamilton depression score or with any of the SADS clinical variables. **Conclusions:** High levels of plasma β -endorphin may be associated with more severe anxiety, phobia, and obsessions/compulsions in depressed patients.*

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Beta-endorphin is a 31-amino-acid hormone released by the pituitary into the systemic circulation in response to various psychological and physiological stimuli (1, 2). High basal plasma levels of β -endorphin and greater than normal secretion of β -endorphin in response to cholinergic stimulation have been observed in previous studies of depressed patients (3, 4), although not in all (5). Adults with affective psychiatric illness and early parental loss have been found to have higher resting plasma levels of β -endorphin than do healthy

comparison subjects with early parental loss (6), and a lower than normal total β -lipotropin/ β -endorphin secretory response after infusion of corticotropin-releasing factor has been found in depressed patients (5). Other studies (7-9) have shown nonsuppression of plasma β -endorphin after dexamethasone administration in depressed patients in whom dexamethasone also did not suppress cortisol, even in patients whose baseline β -endorphin levels were not higher than normal. Postdexamethasone levels of cortisol and β -endorphin were strongly positively correlated (8, 9).

In the present study we tested the hypothesis that high degrees of specific clinical characteristics (symptoms) of depression are associated with higher than normal plasma levels of β -endorphin-like immunoreactivity (referred to here as " β -endorphin"). Using the items involving dysphoric mood and related symptoms from the structured Schedule for Affective Disorders and Schizophrenia (SADS) interview, we examined the following 12 clinical characteristics of depression: somatic anxiety, psychic anxiety, phobia, insomnia, subjective feelings of anger, overt expression of anger, agitation, psychomotor retardation, panic attacks, obsessions/compulsions, appetite loss, and total weight

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loss. Concentration of β -endorphin, severity of depressed mood, and these 12 symptoms were measured in 20 depressed patients and 23 age- and sex-matched comparison subjects.

METHOD

Subjects

The subject group comprised 43 subjects, 20 patients and 23 age- and sex-matched (all male) normal comparison subjects. The patients ranged in age from 29 to 71 years, and the comparison subjects' ages ranged from 31 to 68 years; their mean ages were 43 (SD=11) and 44 (SD=10), respectively ($t=-0.30$, $df=41$, $p=0.8$). They were hospitalized of clinical necessity but on a voluntary basis. All of the patients in the study gave informed consent.

Each patient completed a SADS interview (10) conducted by a research fellow in psychiatry. Twelve individual items from the SADS section on dysphoric mood and related symptoms were chosen. Eight of these items have an interval rating of severity and are parametric variables; the remaining four are nonparametric categorical variables. These items were used in the analyses. (SADS dysphoria items that describe core dysphoria/depression symptoms were not used. Subjective feelings of depression, negative evaluation of self, and similar SADS items were not included because they are so uniformly present in all depressed patients that we felt they would poorly discriminate depression subtypes.)

Research diagnoses were made in a consensus meeting of three psychiatrists and were based on the *DSM-III-R* nosologic system. The diagnoses of the 20 patients were as follows: major depression, recurrent ($N=13$), major depression, single episode ($N=3$), and bipolar disorder not otherwise specified (bipolar II) ($N=4$). All of the patients were currently depressed. Severity of depression was measured with the clinically objective 21-item Hamilton Rating Scale for Depression (11) and the subjective 21-item Beck Depression Inventory (12).

The patients' diagnoses of substance dependence were as follows: no history of alcohol or other substance abuse or dependence ($N=10$), diagnosis of alcohol dependence ($N=4$), alcohol dependence, in remission ($N=2$), alcohol abuse ($N=2$), alcohol abuse, in remission ($N=1$), and amphetamine dependence, in remission ($N=1$). The physical health of each patient was assessed through medical history, physical examination, CBC with WBC differential count, CHEM 20 blood chemistry profile, measurement of serum cholesterol and triglyceride levels, thyroid studies (T_3 , T_4), rapid plasma reagin test for syphilis, urinalysis, and ECG. Patients with medical histories or conditions that may have affected this study were excluded. Some of the subjects involved in this study also volunteered for other studies, which have been described elsewhere (13–18). Although all of the patients had previously

been treated with medication, all were hospitalized and had been free of medication and of alcohol and other substances of abuse for at least 14 days before this study. None of the patients had been treated with fluoxetine, which has a long half-life, before the study.

The 23 comparison subjects were medically and psychiatrically healthy and were recruited from a large metropolitan area. The comparison subjects were not admitted to the hospital, were not currently mentally ill, and had no history of mental illness according to SADS interview. The physical health of each comparison subject was assessed through medical history and CBC with WBC differential count.

β -Endorphin Assay

With standard clinical technique, venous blood was drawn into EDTA anticoagulated tubes. Three different protocols for blood drawing were used over the total time of the study. For 45% of the patients ($N=9$) and 40% of the comparison subjects ($N=9$), a single venipuncture in an antecubital fossa vein provided the single sample used. For 35% of the patients ($N=7$) and 30% of the comparison subjects ($N=7$), a butterfly needle was placed in a forearm vein, and three samples were drawn at 30, 45, and 60 minutes after needle placement. For 20% of the patients ($N=4$) and 30% of the comparison subjects ($N=7$), a blood sample was drawn immediately after butterfly needle placement, followed by samples at 30, 45, and 60 minutes. When multiple samples were drawn, the average β -endorphin level was used in the analysis. No time effect was observed for subjects from whom multiple samples were drawn. The plasma was collected by centrifugation of the blood samples at 400 g for 15 minutes, and it was kept frozen at -80°C until thawed for the β -endorphin radioimmunoassay.

The β -endorphin was measured by using the Nichols solid-phase iodine-125 two-site immunoradiometric assay. All samples were assayed in duplicate and within the same assay. The intra-assay coefficient of variation was 4.4%. The sensitivity of the assay is 10 pg/ml with a 16% cross-reactivity to human β -lipotropin. Two of the depressed patients had β -endorphin levels that were much higher than the others. These samples were assessed again, and similar values were obtained.

Statistical Analysis

The 20 patients and 23 comparison subjects were included in the analyses. For all analyses, a value of $p<0.05$ was considered significant. Differences in degrees of freedom reflect occasional missing data. (Most of the missing data were for the comparison subjects; the majority of these subjects were completely asymptomatic.) Because of the two patients with high β -endorphin levels, the β -endorphin data (in picograms per milliliter) did not fit a normal distribution. After consultation with a statistician, we log normalized the data, and the \log_{10} of each β -endorphin value was used in the

TABLE 1. Levels of β -Endorphin and Continuous Symptom Variables of 20 Depressed Patients and 23 Comparison Subjects

Variable	Depressed Patients		Comparison Subjects		t Test for Independent Samples		
	Mean	SD	Mean	SD	t	df ^a	p
Hamilton depression score ^b	24	10	1	1	10.09	19.60	<0.0009
Beck depression score ^c	21	10	1	1	8.64	18.73	<0.0009
Plasma β -endorphin level (pg/ml)	36.2	48.0	25.4	15.7	0.54	41	0.6
Scores on SADS items							
Somatic anxiety	2.6	1.3	1.1	0.3	4.86	20.32	<0.0009
Psychic anxiety	3.3	1.3	1.4	0.7	3.98	25	0.001
Insomnia	4.2	1.3	1.3	0.5	8.62	24.87	<0.0009
Subjective anger	3.3	1.4	1.5	1.0	4.00	30	<0.0009
Agitation	2.5	1.4	1.0	0.1	4.60	17.00	<0.0009
Psychomotor retardation	3.0	1.3	1.1	0.3	6.18	20.16	<0.0009
Phobia	2.0	1.4	1.2	0.6	2.16	26.34	0.04
Overt anger	2.0	1.2	1.3	0.7	1.68	26	0.1

^aInteger df's are for pooled-variance t tests; noninteger df's are for separate-variance t tests; the separate-variance t test was used when the variances of the two groups were significantly different.

^bOn the 21-item Hamilton Rating Scale for Depression.

^cOn the 21-item Beck Depression Inventory.

TABLE 2. Between-Groups Analyses of Scores on Categorical Symptom Variables of 20 Depressed Patients and 23 Comparison Subjects

SADS Item	Mean Rank ^a		Mann-Whitney U	Wilcoxon Rank Sum W	Correction for Ties	
	Depressed Patients	Comparison Subjects			z	p
Panic attacks	19.68	11.85	63	154	-2.6483	0.008
Obsessions/compulsions	18.89	13.00	78	169	-2.4151	0.01
Appetite	20.26	11.00	52	143	-3.2486	0.001
Weight loss	18.94	11.92	64	155	-2.4218	0.01

^aRank in nonparametric statistical test.

TABLE 3. Correlations of β -Endorphin Level With SADS Symptom Scores for Combined Depressed and Comparison Subjects and for Depressed Patients

Group and SADS Item	Correlation of β -Endorphin Level With SADS Item Score		
	r	df	p
All subjects (N=43)			
Psychic anxiety	0.42	25	0.03
Phobia	0.44	30	0.01
Somatic anxiety	0.32	30	0.07
Panic attacks	0.30	30	0.09
Obsessions/compulsions	0.30 ^a	30	0.09
Depressed patients (N=20)			
Psychic anxiety	0.58	16	0.01
Phobia	0.58	17	0.009
Obsessions/compulsions	0.49 ^a	17	0.03
Somatic anxiety	0.40	17	0.09

^aSpearman's rank-order correlation coefficient for nonparametric (categorical) variables.

statistical analyses. All statistics were calculated by using standard statistical programs (19, 20).

We used t tests for independent samples to test for the significance of the between-groups differences in the continuous variables, and the Mann-Whitney U/Wilcoxon rank sum W test or the Kruskal-Wallis one-way analysis of variance (ANOVA) and chi-square analysis were used for between-groups differences in the categorical variables (panic attacks, obsessions/compulsions, appetite loss, and total weight loss).

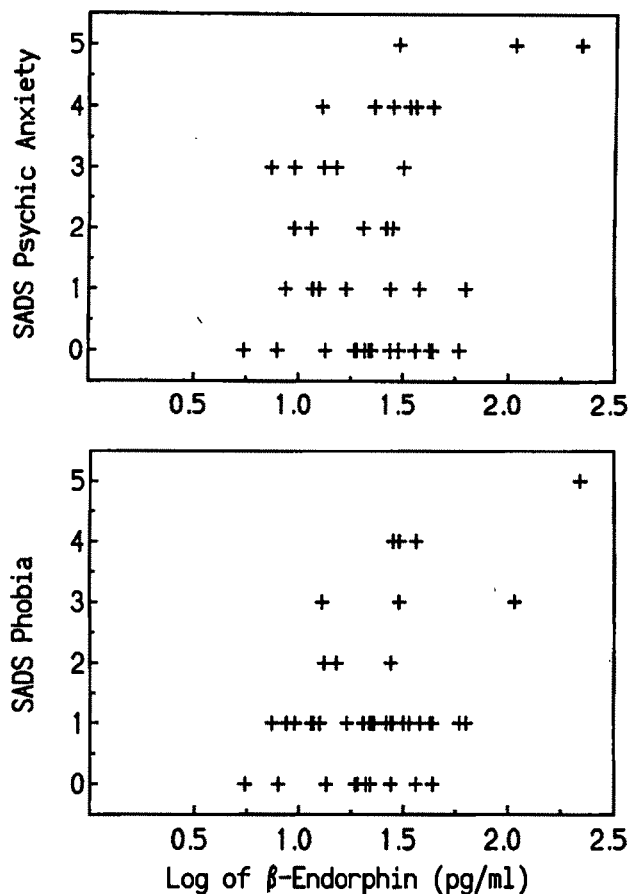
Parametric correlations of the continuous variables were calculated by using Pearson's correlation coefficient (r), and nonparametric correlations of the categorical variables were calculated with Spearman's rank-order correlation coefficient (r_s).

RESULTS

Characteristics of the two groups are shown in table 1. The Hamilton and Beck depression scores of the two groups were markedly and significantly different. Although the patients had a higher mean plasma β -endorphin level than the comparison subjects, the difference did not reach significance.

There were significant differences in the scores of the two groups on 11 of the 12 SADS mood items that clinically characterize depression; the patients had significantly more severe somatic anxiety, psychic anxiety, insomnia, subjective feelings of anger, agitation, psychomotor retardation, phobia, panic attacks, and obsessions/compulsions than the comparison subjects (see tables 1 and 2), but the patients did not have significantly more overt expressions of anger. Table 2 presents the results of the Mann-Whitney U/Wilcoxon rank sum W test for panic attacks, obsessions/compulsions, appetite, and weight loss. In addition to significantly more panic attacks and obsessions/compulsions, the patients showed significantly poorer appetite and greater total weight loss.

FIGURE 1. Relation of β -Endorphin Level to SADS Psychic Anxiety and Phobia Scores for Combined Depressed and Comparison Subjects (N=43)^a



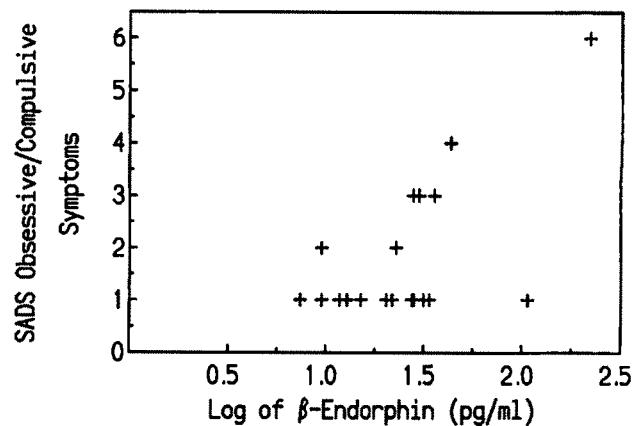
^aSignificant correlations for both psychic anxiety ($r=0.42$, $df=41$, $p=0.03$) and phobia ($r=0.44$, $df=41$, $p=0.01$).

Within the group of all 43 subjects, β -endorphin concentration correlated significantly with psychic anxiety and with phobia (table 3 and figure 1). There was no significant correlation in this group between β -endorphin and score on the Hamilton or Beck depression scale or any of the other SADS items assessed, although a nearly significant difference was found for somatic anxiety, for panic attacks, and for obsessions/compulsions (table 3).

Within the group of the 20 patients, β -endorphin correlated significantly with psychic anxiety, with phobia, and with obsessions/compulsions (table 3 and figure 2). There was not a significant correlation between β -endorphin and Hamilton or Beck depression score or score on any of the other SADS items, although a nearly significant correlation was found for somatic anxiety (table 3). Within the group of all 23 comparison subjects, there were no significant correlations between β -endorphin and any of the SADS variables.

The 10 patients with histories of recent or past substance abuse were examined separately to see whether substance abuse history affected the interaction be-

FIGURE 2. Relation of β -Endorphin Level to SADS Obsessions/Compulsions Score for 20 Depressed Patients



tween β -endorphin and the relevant SADS variables. Age, Hamilton score, Beck score, β -endorphin level, and scores for somatic anxiety, psychic anxiety, phobia, and obsessions/compulsions were not significantly different between the patient groups with and without histories of substance abuse (see table 4). For the nonparametric variable, obsessions/compulsions, the results of Kruskal-Wallis one-way ANOVA and chi-square analysis were as follows: patients *with* substance abuse history, mean rank=10.17; patients *without* substance abuse history, mean rank=9.85 ($\chi^2=0.02$, $df=1$, $p=0.8$, n.s.). For the 10 patients with substance abuse histories, β -endorphin did not significantly correlate with any of the other variables ($0.1 < p < 0.7$).

DISCUSSION

This study, designed to test the hypothesis that plasma β -endorphin concentration in depressed patients is associated with specific clinical characteristics of depression, demonstrated a significant association between β -endorphin and three specific symptoms of depression as elicited by SADS interview—psychic anxiety, phobia, and obsessions/compulsions—and further suggested a possible association between β -endorphin and somatic anxiety and panic attacks.

Except for overt expressions of anger, the groups were significantly different in the symptoms chosen for study. There were no significant correlations between β -endorphin and the SADS interview items in the comparison group. This finding may support the specificity of the association between β -endorphin and anxiety, phobia, and obsessions/compulsions in the patients. An equally likely explanation, however, is that the narrow range of responses by the comparison subjects to the SADS items (most were scored zero) made it difficult to find significance on statistical tests for correlations.

The β -endorphin level was higher in the patient group but not significantly so. The literature is currently in conflict as to the true association between depression

TABLE 4. Age, β -Endorphin Level, and Selected Symptom Scores of 20 Depressed Patients With and Without Histories of Substance Abuse

Variable	With Abuse History (N=10)		Without Abuse History (N=10)		ANOVA		
	Mean	SD	Mean	SD	F	df	p
Age (years)	40	9	47	13	2.88	1, 17	0.1
Hamilton depression score ^a	23	8	26	13	0.002	1, 17	0.9
Beck depression score ^b	19	11	22	10	0.54	1, 17	0.5
Plasma β -endorphin level (pg/ml)	30.7	29.1	41.7	62.9	0.68	1, 17	0.4
Scores on SADS items							
Somatic anxiety	2.8	1.2	2.4	1.3	0.97	1, 16	0.3
Psychic anxiety	3.5	1.4	3.1	1.2	0.42	1, 16	0.5
Phobia	2.0	1.3	2.0	1.5	0.03	1, 16	0.9

^aOn the 21-item Hamilton Rating Scale for Depression.^bOn the 21-item Beck Depression Inventory.

and β -endorphin (3, 4, and 6 versus 5, 7–9). This conflict may have resulted from inattention to specific symptoms characterizing depression.

The results support the concept that β -endorphin is associated with specific clinical symptom clusters in depression, specifically symptoms associated with anxiety states. The results support the recent conceptualization of broad overlap between the depression spectrum of illnesses and the anxiety disorders. Anxiety and depression may have a common neurological substrate (21). In multivariate genetic analysis (22), no evidence could be found for genes that specifically affect symptoms of depression without also strongly influencing symptoms of anxiety. In a recent study of twin pairs (23), the results suggested an etiologic relationship between mixed major depression/anxiety disorders and major depression. Patterns of relationships of anxiety and depression to sociodemographic factors, prior psychopathology, and life events do not distinguish the two syndromes (24), and most widely used assessment methods do not measure anxiety and depression independently (25). Almost 40% of patients with *DSM-III* anxiety disorders simultaneously fulfill the criteria for a depressive disorder, mainly major depression (26). Lactate-infusion-induced decreases in β -endorphin have not distinguished subjects with major depression from subjects with panic disorder (27). Symptom overlap between depression and anxiety is large. The probability of symptom overlap in 150 psychiatric outpatients has been found to be 56%–60% (28). Finally, in a study of physically active versus sedentary men (29), the physically active men had a lower mean plasma β -endorphin level, lower anxiety index, and lower depression score than did the sedentary men. The literature regarding the relation of anxiety to depression has been reviewed by Stavrakaki and Varge (30).

Future studies may explore hypotheses concerning the specific role of β -endorphin in anxiety and phobia within the context of depression. Further, there is a growing interest in defining specific mental illnesses in terms of biological substrates rather than clusters of clinical symptoms or "phenotypic expression." The mapping of biological markers with clinical symptoms is a necessary step in this nosologic progress.

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Neuroendocrine Effects of Intravenous Clomipramine in Depressed Patients and Healthy Subjects

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***Objective:** Neuroendocrine challenge paradigms have been used to assess serotonergic systems in depression, but limitations in the specificity of many of these tests have been noted. In this study, the neuroendocrine responses to acute intravenous administration of the serotonin (5-HT) reuptake inhibitor clomipramine were assessed in depressed patients and matched control subjects. **Method:** Thirty hospitalized patients who met DSM-III-R criteria for major depression, and 30 healthy control subjects who were matched for age, sex, and season of year for the time of study, received 12.5 mg of intravenously administered clomipramine. **Results:** The depressed patients demonstrated significant blunting of prolactin responses to clomipramine, as well as trends toward blunted ACTH and cortisol responses. There was no difference between the patient and control groups in growth hormone responses, plasma clomipramine levels, or self-reports of side effects. **Conclusions:** These data support the hypothesis that depressed patients have abnormal neuroendocrine responses to the intravenous administration of the 5-HT reuptake inhibitor clomipramine. Further study is required to delineate the mechanisms responsible for the abnormal response to intravenously administered clomipramine in depression.*

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Neuroendocrine challenge paradigms, which measure changes in plasma concentrations of serotonin (5-HT)-responsive hormones following exposure to 5-HT agents, have provided support for the indolamine hypothesis of depression (1). Several groups of investi-

gators have reported blunted prolactin responses to the 5-HT-releasing agent/uptake inhibitor fenfluramine and to the 5-HT amino acid precursor L-tryptophan in depressed patients (2-7). The cortisol response to the precursor 5-hydroxytryptophan is exaggerated in depressed patients, and the magnitude of the 5-hydroxytryptophan cortisol response is significantly correlated with severity of depression and suicidal activity (8, 9). Thus, depressed patients demonstrate abnormal neuroendocrine responsivity to pharmacologic stimulation of central 5-HT systems.

There are limitations, however, to the conclusions that can be drawn from these studies. First, the specificity of each of these probes for 5-HT systems has been questioned (10). Fenfluramine, for example, causes the release of dopamine and norepinephrine, as well as 5-HT (11), and can provoke substantial side effects (5), which might in turn stimulate the release of prolactin and other stress-responsive hormones. The *d*-isomer appears to be more specific for 5-HT effects and to have a milder side effect profile than the more commonly used racemic compound. However, in the only study to date to use *d*-fenfluramine (5), the compound was administered orally, thereby introducing the pharmacokinetic limitations described later in this paper. Trypto-

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phan competes with tyrosine for a shared carrier mechanism to cross the blood-brain barrier (12) and thus might indirectly affect central catecholaminergic function by decreasing the availability of catecholamine precursor. Like fenfluramine, tryptophan can provoke side effects (7, 13), which might in turn stimulate stress-mediated release of prolactin and other neurohormones. The uptake of 5-hydroxytryptophan is not limited to 5-HT neurons (14, 15); 5-hydroxytryptophan can be converted into 5-HT in catecholaminergic neurons, leading to the release of catecholamines by displacement (16).

Pharmacokinetic factors can also affect neuroendocrine challenge tests, especially those which use the oral administration of the challenge agent (17). Since the neuroendocrine response data are collected at timed intervals, even relatively modest differences in the rate and/or degree of absorption of the challenge agent can contribute substantially to the variance observed. For example, the finding of blunted prolactin responses to tryptophan in depressed patients was not replicated in a study that controlled for plasma tryptophan concentrations in the data analysis (18).

The 5-HT uptake inhibitor clomipramine has considerable utility as a 5-HT challenge agent (19). Clomipramine is a potent inhibitor of 5-HT uptake at concentrations that have little effect on norepinephrine, although its demethylated metabolite does inhibit norepinephrine reuptake (20). Intravenous administration of clomipramine minimizes the problems seen with oral pharmacologic challenges regarding interindividual differences in rate and degree of absorption. Furthermore, this type of administration avoids the "first pass" effect of hepatic metabolism and thereby delays the formation of demethylated clomipramine and minimizes its effect on norepinephrine during the period of hormonal measurements (19). In the present study we chose to apply the clomipramine challenge test to hospitalized depressed patients and matched healthy control subjects.

METHOD

Subjects

This study was approved by the University of North Carolina School of Medicine Committee for the Protection of the Rights of Human Subjects. Oral and written informed consent was obtained from all subjects before their enrollment in the study. All potential subjects received a comprehensive medical evaluation, and only those who were free of any medical condition that could either jeopardize their safety or complicate the interpretation of the data were eligible to participate.

We studied 30 depressed patients (11 men and 19 women) who were hospitalized at a university hospital or on the university's clinical research unit at a psychiatric hospital. The mean age of the patients was 31.6 years (SD=10.5) (range=18–61 years). All patients were free of psychoactive medication for a minimum of 2 weeks at the time of testing. Diagnoses were assigned

by a board-certified psychiatrist (R.N.G.) and were based on all available clinical data, including the information generated by the semistructured Schedule for Affective Disorders and Schizophrenia—Lifetime Version (SADS-L) (21), and without knowledge of the results of clomipramine testing. All patients met DSM-III-R criteria for major depressive episode; three patients had bipolar disorder, depressed phase, and the remaining patients met criteria for major depression, single episode (N=12) or major depression, recurrent (N=15). The mean score on the 21-item Hamilton Rating Scale for Depression (22) at baseline, before the test procedure, was 24.4 (SD=6.0) (range=16–40).

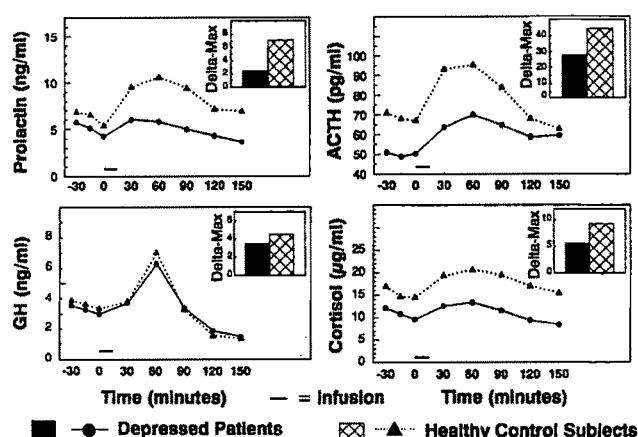
Healthy control subjects were recruited through printed advertisements distributed throughout the university campus and placed in the local and student newspapers. All potential control subjects underwent careful medical and psychiatric screening, including the administration of the SADS-L (21). Only subjects with no personal history of psychiatric illness and no family history of mood disorders and alcoholism were eligible. Control subjects were free of exposure to psychoactive medications and alcohol for a minimum of 3 weeks before the study. Eleven male and 19 female volunteers were selected in an effort to match the age of the depressed subjects as closely as possible. The mean age of the volunteers was 29.3 years (SD=7.1) (range=19–50 years). There was no significant difference in mean age between the groups ($t=0.96$, $df=50.9$, $p=0.34$).

The control subjects were admitted to the general clinical research center of a university hospital, where their infusion studies were performed. Because of recent reports of seasonal variation in some indices of serotonergic function (23), the studies of the control subjects were scheduled to match the seasonal distribution of the depressed patients' infusions. Fisher's exact test confirmed that there was no significant difference in the seasonal distribution of the testing of depressed and control subjects ($p=1.00$).

Infusion Procedures

Subjects were placed on a standard low monoamine, caffeine-controlled diet (24) for 3 days before the study. All subjects maintained a fasting state (except for water) beginning at midnight the night before the procedure and continuing until after the last blood specimen had been obtained. Subjects were awakened at 7:00 a.m. on the day of the infusion and were allowed to get out of bed at that time for a brief period to micturate if necessary. After that, each subject remained at strict bed rest until the procedure was completed. A research nurse determined that subjects did not fall asleep during the procedure.

An intravenous line was started at 8:30 a.m. in an antecubital vein and kept patent with a slow drip of normal saline solution. Blood samples were obtained 30, 45, and 60 minutes after insertion of the intravenous line for determination of baseline hormone concentrations. Immediately after the collection of the last baseline

FIGURE 1. Hormone Responses to Intravenous Administration of Clomipramine in 30 Depressed Patients and 30 Healthy Control Subjects

sample, 100 cc of normal saline containing 12.5 mg of clomipramine were infused over a 15-minute period. Additional blood samples were obtained 30, 45, 60, 90, 120, and 150 minutes after the start of the infusion.

Blood pressure and pulse were measured and recorded at each sampling point throughout the procedure with an automated machine (Criticon, Tampa, Fla.). Visual 100-mm analog scales were used to evaluate six different subjective states (best ever/worst ever, calm/restless, energetic/tired, happy/sad, most/least anxious, and most/least nauseated).

Collection and Assay Techniques

Blood samples were drawn into disposable polypropylene syringes and transferred to heparinized polypropylene tubes (a portion of each sample was placed into EDTA treated glass tubes for ACTH measurement). The samples were immediately placed on ice and promptly centrifuged at 4 °C, and the resultant plasma was stored at -70 °C.

Plasma prolactin and growth hormone concentrations were measured with double antibody radioimmunoassays, which used commercial reagents (Becton Dickinson, Orangeburg, N.Y.; Kallestad Diagnostics, Austin, Tex.). The sensitivities of the prolactin and growth hormone assays were 1.0 ng/ml and 0.2 ng/ml, respectively; the intra-assay and interassay coefficients of variation were 5% and 9% for prolactin and 4% and 7% for growth hormone. Plasma cortisol concentrations were assayed by radioimmunoassay with commercial reagents (Becton Dickinson). The sensitivity of the assay was 0.04 μg/dl, with intra-assay and interassay coefficients of variation of 5% and 7%. Plasma ACTH concentrations were measured by radioimmunoassay with commercial reagents (ICN Biochemicals, Los Angeles). The sensitivity of the assay was 10 pg/ml, and the intra-assay and interassay coefficients of variation were 5% and 7%.

Plasma clomipramine and demethylated clomipramine concentrations were measured by using high per-

formance liquid chromatography with ultraviolet detection, using a modification of a previously described technique (25). Each 0.1 ml-plasma sample was placed in a polypropylene capped conical tube and 50 ng of imipramine (internal standard) in methanol was added, along with 1.0 ml of hexane:isoamyl alcohol (9:1) and 0.01 ml N NaOH. After shaking and centrifuging (5 minutes each), the organic layer was transferred to a clean tube. The organic solution was then evaporated under a stream of nitrogen at ambient temperature, the residue was resuspended with 0.1 ml of mobile phase, and 0.08 ml was injected into the column. The chromatographic system consisted of a silica column (Keystone Scientific, Bellefonte, Pa.), a mobile phase of acetonitrile:methanol:8.5 N ammonium hydroxide (83.3%:16.3%:0.4%) at a gradient flow of 1 to 4 ml/minute, and ultraviolet detection at 214 nm. Twenty to 30 samples were processed simultaneously, including eight to 10 samples to which known amounts of the drugs had been added for construction of a calibration curve. The lower limits of detection were 10 ng/ml for clomipramine and demethylated clomipramine, and the intra-assay and interassay coefficients of variation were between 4% and 10%.

Statistical Analyses

All hormone values were log-transformed to stabilize variances and to approximate normal distributions before the analyses, since the raw hormone values had a strong positive skew; for clarity of presentation, however, raw (i.e., nontransformed) values are presented in figure 1 and in the Results section. The last hormone value before clomipramine infusion was considered to be the baseline value for the purpose of comparison to postinfusion values. Our primary index of hormonal responsivity to clomipramine was defined as the maximum postinfusion change from baseline, or Δ_{max} . Type 1 errors for maximum change were controlled at 5% for each hormone. Because our age match was not exact, we controlled for age in all analyses of maximum change by using one-way analysis of covariance (ANCOVA).

Supplementary analyses used two-way ANCOVA for repeated measures (with age as a covariate), with the Greenhouse-Geisser adjustment for autocorrelation in the data (usually resulting in fractional degrees of freedom). This repeated measures ANCOVA was applied directly to the baseline and the five postinfusion values to assess overall group differences, including any baseline discrepancy between groups. We also applied repeated measures ANCOVA to the five postinfusion changes from baseline to assess the significance of Group by Time interaction in clomipramine responsivity, after controlling for nonsignificant baseline differences. Variables analyzed by repeated measures ANCOVA consisted of the log-transformed values for plasma concentrations of each of the four hormones (prolactin, ACTH, cortisol, and growth hormone), the nontransformed cardiovascular measures

(systolic blood pressure, diastolic blood pressure, and pulse rate), the subjects' response on the six 100 mm-line visual analog scales, and plasma clomipramine concentrations.

Student's *t* test was used to compare mean age and baseline hormone and cardiovascular measures between the groups. Fisher's exact test was used to compare groups with respect to the season during which the clomipramine infusions were given.

These analyses were performed with the Statistical Analysis System software package (26). All *p* values are two-tailed.

RESULTS

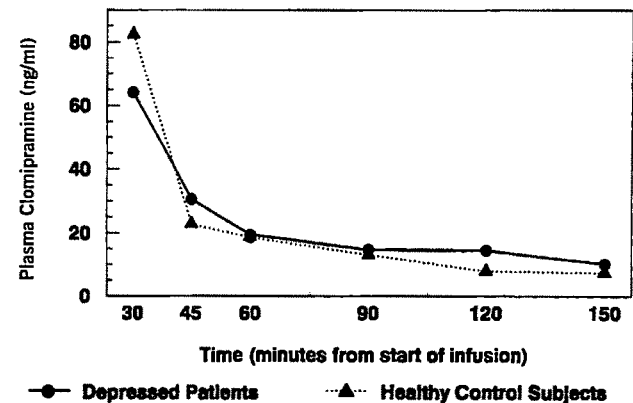
The baseline plasma hormone concentrations and cardiovascular measures were not significantly different in depressed patients and control subjects. However, there were trends toward lower levels of prolactin ($t=1.8$, $df=58$, $p<0.08$), ACTH ($t=1.5$, $df=58$, $p<0.16$), and cortisol ($t=1.3$, $df=58$, $p<0.20$) and higher pulse ($t=1.8$, $df=58$, $p<0.09$) in the former group.

The prolactin response to clomipramine was blunted in depressed patients compared to the control subjects. The change in prolactin level was smaller in the former group than in the latter (Δ_{\max} prolactin=2.4 ng/ml, $SD=4.0$, and 7.1, $SD=10.1$; $F=7.7$, $df=1$, 57, $p<0.008$, ANCOVA). ANCOVA confirmed a significant difference in the prolactin response to clomipramine in the depressed patients and control subjects (for Group effect: $F=6.8$, $df=1$, 52, $p<0.02$) (figure 1).

The cortisol and ACTH responses tended to be lower in depressed patients than in control subjects, although these trends did not achieve statistical significance (figure 1). The change in cortisol level was smaller in depressed patients than in healthy subjects (Δ_{\max} cortisol=5.5 μ g/ml, $SD=6.4$, and 9.2, $SD=8.9$; $F=3.8$, $df=1$, 57, $p<0.06$, ANCOVA). Repeated measures ANCOVA revealed a significant Group effect ($F=8.0$, $df=1$, 52, $p<0.007$), reflecting a trend toward a difference at baseline that persisted over time; Group by Time effect did not reach significance ($F=2.0$, $df=2.1$, 111, $p<0.14$). The change in ACTH showed considerable variance within each group, and while the mean value was lower in the depressed group than in the control subjects, the difference was not significant (Δ_{\max} ACTH=27.7 pg/ml, $SD=34.6$, versus 43.9, $SD=75.1$; $F=0.2$, $df=1$, 57, $p>0.63$, ANCOVA). Repeated measures ANCOVA demonstrated a trend toward Group ($F=1.1$, $df=1$, 51, $p<0.31$) and Group by Time ($F=1.4$, $df=2.1$, 111, $p<0.26$) effects, although these trends failed to reach statistical significance.

Depressed patients and control subjects did not demonstrate a substantial difference in growth hormone responses to clomipramine (Δ_{\max} =3.5 ng/ml, $SD=9.1$, and 4.5, $SD=8.5$; $F=0.8$, $df=1$, 57, $p<0.40$, ANCOVA) (figure 1), and repeated measures ANCOVA did not suggest a significant Group effect ($F=0.1$, $df=1$, 53, $p>0.79$).

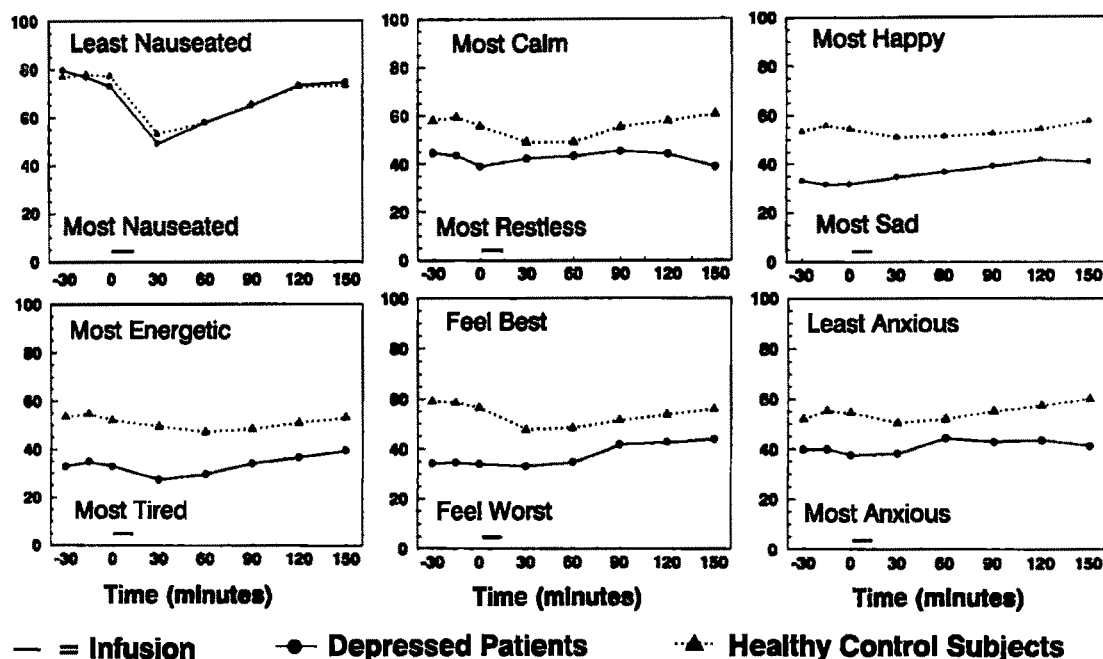
FIGURE 2. Plasma Clomipramine Concentrations in 30 Depressed Patients and 30 Healthy Control Subjects



Plasma clomipramine concentrations were not significantly different in depressed patients and healthy subjects (repeated measures ANCOVA for Group effect: $F=1.1$, $df=1$, 49, $p>0.30$; for Group by Time effect: $F=0.4$, $df=1.5$, 90.5, $p>0.66$) (figure 2). Demethylated clomipramine was not detected in any of the samples.

Both depressed patients and control subjects demonstrated a brief, modest increase in self-reports of nausea after clomipramine infusion, with a return to baseline. There was no significant difference between the groups in terms of nausea self-reports, with minimal Group (repeated measures ANCOVA: $F=0.1$, $df=1$, 57, $p>0.79$) and Group by Time (repeated measures ANCOVA: $F=0.6$, $df=2.6$, 148.0, $p>0.57$) effects. As anticipated, the self-report scores for mood variables were different in patients and control subjects; the former group was more sad and more anxious, felt worse, and was less calm and more tired than the latter (repeated measures ANCOVA Group effects for these self-reports: $F=17.9$, $df=1$, 57, $p=0.0001$; $F=7.7$, $df=1$, 57, $p<0.008$; $F=12.2$, $df=1$, 55, $p<0.001$; $F=5.3$, $df=1$, 5, $p<0.03$; $F=28.4$, $df=1$, 57, $p=0.0001$). There were no significant Group by Time effects in the first three of these mood variables (for sad/happy, least/most anxious, and feeling best ever/feeling worst ever, repeated measures ANCOVA: $F=1.1$, $df=3.1$, 175.3, $p>0.35$; $F=1.6$, $df=2.9$, 162.9, $p>0.19$; $F=1.3$, $df=2.8$, 151.7, $p>0.27$, respectively). There were significant Group by Time effects for most/least calm (repeated measures ANCOVA: $F=4.3$, $df=2.8$, 160.2, $p<0.008$) and feeling most tired/most energetic ($F=2.7$, $df=2.9$, 164.4, $p<0.05$). Depressed patients demonstrated a very modest increase in self-reported calmness and a modest decrease in self-reported tiredness, followed by a return to baseline after clomipramine; control subjects demonstrated a modest decrease in self-reported calmness, followed by a return to baseline, and a very modest, sustained decrease in self-reports of feeling energetic (figure 3). There were no significant group differences in systolic blood pressure, diastolic blood pressure, or pulse after clomipramine infusion (data not shown).

FIGURE 3. Self-Report Scores for Side Effects and Mood States in 30 Depressed Patients and 30 Healthy Control Subjects After Intravenous Administration of Clomipramine



DISCUSSION

The most striking finding to emerge from this study is the blunted prolactin response to intravenous clomipramine in depressed patients. Blunted prolactin responses to various serotonergic probes, including tryptophan (6, 7), fenfluramine (2–5), and now clomipramine, have been observed in depression. While the finding of less prolactin responsivity to serotonergic agents in depressed patients is quite consistent, the interpretation and physiologic bases for these phenomena are not clear. Two important questions need to be considered: Is a given neuroendocrine probe a valid measure of central 5-HT systems? What specific mechanisms are responsible for the abnormal neuroendocrine responses in depressed patients?

Neuropharmacologic probes for 5-HT are predicated on the assumption that the dependent variable, i.e., the hormone that is measured before and after administration of the 5-HT stimulus, is regulated by central 5-HT systems. In fact, the neuroregulation of these anterior pituitary peptides is quite complex; 5-HT plays a role, but so do other neurotransmitters (see reference 27 for a comprehensive review). The goal, therefore, in developing a neuroendocrine probe for 5-HT is to find a challenge agent that affects 5-HT but does not directly affect other neurotransmitters. Even with an ideal, specific 5-HT probe, however, interpretation of results must be tempered by the implications of the multiple neurotransmitter regulation of hormone release. For example, a blunted prolactin response to clomipramine could be related to enhanced tuberoinfundibular dopaminergic activity that 5-HT stimulation is unable to overcome. Arguing against this interpretation is the ob-

servation by Anderson and Cowen (28) that the prolactin response to the dopamine antagonist metoclopramide is not different in depressed patients and control subjects.

All of the currently available 5-HT neuroendocrine probes, including the clomipramine challenge test described in this report, have potential limits regarding their specificity for 5-HT systems. While clomipramine is a fairly potent 5-HT reuptake inhibitor with minimal effects on norepinephrine, its desmethyl metabolite does inhibit norepinephrine uptake (20). In this regard, it is encouraging to note that we were unable to detect demethylated clomipramine in any of our samples, using an assay with a sensitivity of 10 ng/ml. Laakmann's group (29–31) has also found consistent prolactin effects from intravenous clomipramine, although Filip et al. (32) did not in a small study using a lower dose than that employed in the present study.

Like other pro-serotonergic agents, clomipramine administration was associated with nausea, but the amount was mild in our subjects and did not evoke other signs of nonspecific stress (e.g., increased pulse). Perhaps a certain degree of nausea may be inevitable whenever 5-HT stimulation that is sufficient to produce neurohormone release occurs; an emesis center that is partly under 5-HT control may be present in humans. In this study, it is important to note that the self-report ratings of nausea were nearly identical in patients and control subjects, so that nausea per se cannot account for the differences in prolactin release that occurred in the two groups.

The mechanisms responsible for the blunted prolactin responses in depressed patients may differ for the various 5-HT probes (e.g., tryptophan, fenfluramine,

clomipramine). One possible mechanism that has to be considered is a defect in the secretory capacity of anterior pituitary lactotrophs. Some investigators have reported blunted prolactin responses to a variety of challenges, including thyrotropin-releasing hormone (TRH) (33, 34), narcotics (35, 36), and insulin-induced hypoglycemia (37), as well as diminished basal prolactin levels (33, 34) in depressed patients, although the latter finding has not been replicated consistently (38–41). However, we have found that a group of seven depressed patients with blunted prolactin responses to clomipramine were able to mount robust prolactin responses to TRH stimulation (42). Thus, the blunted prolactin response to clomipramine does not appear to be the consequence of diminished lactotroph secretory capacity.

If, in fact, the diminished prolactin response to clomipramine is a reflection of an abnormality in central 5-HT systems, the specific nature of the abnormality remains to be elucidated. Presynaptic alterations may play a role. Delgado et al. (43) have recently demonstrated that acute tryptophan depletion can precipitate the reemergence of depressive symptoms in remitted patients; perhaps similar presynaptic defects could account for some of the neuroendocrine stigmata of depression as well, including the abnormal neurohormone response to clomipramine reported here.

Postsynaptic mechanisms must be considered in the interpretation of these results as well. It is not clear which postsynaptic 5-HT receptor subtype is involved in prolactin regulation. Both 5-HT_{1A} (44) and 5-HT₂ (45–48) receptors have been implicated. Further clarification of the specific mechanisms by which 5-HT affects normal prolactin release might provide important clues regarding the pathophysiologic bases for the abnormal prolactin responses to clomipramine in depression.

The hypothalamic-pituitary axis is also regulated by 5-HT, and we observed trends toward lower ACTH and cortisol responses to clomipramine in depressed patients. The mechanism by which 5-HT affects the hypothalamic-pituitary axis is not clear, although it appears that 5-HT_{1A} receptors play a role (49, 50). As Meltzer has pointed out (51), it is possible that prolactin and cortisol are controlled by separate serotonergic systems that differ in their overall pattern of function. In the rat, there are data that suggest that 5-HT-dependent increases in corticosterone and prolactin are mediated by different neuronal mechanisms (52). Thus, more work is necessary in order to delineate the physiologic bases for our observations.

Our findings of a blunted prolactin response and trends toward blunting in the ACTH and cortisol response to clomipramine are consistent with the results of an earlier pilot study (53), which was conducted at a different site and used a somewhat lower clomipramine dose (i.e., 10 mg). In contrast, however, we detected an exaggerated growth hormone response to clomipramine in that earlier study, yet found no significant abnormality in the growth hormone response to clomipramine in depressed patients in the present investiga-

tion. In our previous study, we noted that the abnormal growth hormone response could be accounted for by extremely robust responses in three of the seven depressed patients. Our speculation regarding erratic growth hormone release in depression, perhaps as a consequence of noradrenergic dysregulation, remains the most conservative explanation of that earlier finding, which failed to reemerge in this larger, more controlled study.

Recently, Jarrett et al. (54) reported finding no difference in sleep-related prolactin responses to intravenous clomipramine in depressed outpatients and healthy subjects. Several important methodological differences may have contributed to this apparent discrepancy between their findings and our results. First, as Jarrett et al. point out, the hormonal response pattern to a provocative stimulus will vary during the day, and for many hormones, there is a diurnal sensitivity to pharmacologic stimuli consistent with differences in neurotransmitter tone over the course of the day. Second, the experimental (depressed) and control subjects in the Jarrett et al. study were not matched for age or sex. For example, the control group was significantly younger than the patient group (30.3 versus 42.4 years; $p=0.01$). Since we have found that younger healthy subjects have significantly lower prolactin responses to clomipramine than older healthy subjects (55), the younger age of Jarrett et al.'s control group could account for the lack of observed blunting in the depressed group. Finally, the sample size in the Jarrett et al. study was so small (eight depressed patients and five healthy control subjects) that their power to detect a difference between groups comparable to the difference we report here (i.e., standardized effect size, $d=0.74$) was only 20%.

Given the complexity of the neurochemical systems that regulate pituitary hormone release, the precise mechanisms responsible for the abnormal neuroendocrine profile seen in depressed patients after clomipramine challenge are not yet defined. We believe that these findings are related to dysregulation of central serotonergic systems in depression. However, additional investigations will be necessary to test this hypothesis and to clarify further the nature of such dysregulation.

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Prevalence of Seasonal Affective Disorder in Alaska

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Objective: The goals of this study are to provide estimates of the prevalence of seasonal affective disorder in Alaska, to examine sociodemographic correlates, and to evaluate the relation between seasonal affective disorder and general depression. **Method:** A random sample of 283 residents of Fairbanks who had lived in Alaska for 3 years or more were interviewed with the Seasonal Pattern Assessment Questionnaire and the Center for Epidemiologic Studies Depression Scale (CES-D Scale). **Results:** Twenty-six (9.2%) of the subjects met diagnostic criteria for seasonal affective disorder, one of the highest figures yet reported. These cyclic winter affective disorders occurred more often in women than men (ratio=3:2) and were less prevalent among residents who were older than 40 years of age. Assessment of depression with the CES-D Scale supported the diagnostic classification of respondents and the differentiation of seasonal affective disorder from other depression. **Conclusions:** This study supports the conclusions that seasonal affective disorder is prevalent in northern populations and that sex and age may represent the major risk factors that differentiate it from the general experience of depression in northern communities.

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The darkness, cold, and isolation then drive the mental faculties on to melancholy . . . The earliest effects become manifest in the mental realm. The physical changes become evident slowly, often not at all until near the end or at sunrise of the next year.

—Dr. Frederick Cook, circa 1897 (1, pp. 113, 115)

Seasonal changes in mood and energy have long been accepted as a feature of life in the far north, and Dr. Cook was one of the early medical observers who described such effects. With the introduction of the diagnosis of seasonal affective disorder (2, 3), questions about the incidence and prevalence of seasonal mental health problems have been raised. This study provides estimates of the prevalence of seasonal affective disorder in Alaska, examines sociodemographic correlates, and evaluates the relation between seasonal affective disorder and general depression.

BACKGROUND

Seasonal affective disorder (major depression, seasonal pattern, in *DSM-III-R*) has been characterized by

onset during autumn of depressive symptoms with an atypical pattern, featuring hypersomnia, irritability, weight gain, and carbohydrate craving. Among clinical populations the syndrome is more common in women, in a ratio of about 4:1 (4), which is higher than the 2:1 ratio noted in depressive illness in general (5). Clinical histories of patients receiving phototherapy for seasonal affective disorder suggest that depressive episodes last longer the farther north the patients live (4).

In a random mail survey of 400 New York City residents (6), seasonal symptoms were common among the 193 respondents. Wintertime fatigue was reported by 50%, winter weight gain by 47%, increased sleep by 42%, and decreased social activity by 31%; 31% of the respondents said they felt worse in the winter.

Among the 383 subjects who responded to a telephone survey of 416 randomly chosen residents of Montgomery County, Md. (7), seasonal affective disorder was estimated at 4.3% (71% female) and subsyndromal seasonal affective disorder (milder complaints) at 13.5% (55% female). Clinical interviews with a 10% subsample of the respondents revealed that the designations of no seasonal affective disorder, subsyndromal seasonal affective disorder, and seasonal affective disorder were consistent with levels of depression measured with the Hamilton Rating Scale for Depression (8, 9).

A random mail survey of 1,576 residents at four different latitudes in the United States (10) produced estimates for seasonal affective disorder ranging from 1.4% in Sarasota, Fla., to 9.7% in Nashua, N.H. Response rates for the four sites ranged from 40.1% to 60.5%.

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Clinical studies of seasonal affective disorder in Alaska have been completed, but no epidemiologic data have been available (4, 11). Fairbanks lies at a latitude of 64° north, presenting an environment of extreme seasonal contrasts. Available daylight at winter solstice is approximately 3 hours and 42 minutes, but at summer solstice the available daylight is 21 hours and 49 minutes. This provides opportune conditions under which to assess the relation between extreme seasonal changes and depression.

METHOD

Subjects

This study of the prevalence of seasonal affective disorder was part of a larger community health survey based on standardized household interviews administered from mid-January through mid-March to a multistage area probability sample of 283 adult (21 years or older) residents of Fairbanks, Alaska (total population=75,000). Potential subjects who were living on military bases, on university campuses, or within hospitals, nursing homes, etc., were not included. In addition, only those respondents who had lived in Alaska for 3 years or more were included to ensure sufficient exposure to the seasons there to establish a repeated seasonal pattern of related symptoms. The 283 subjects who participated in the interviews represented 91% of all respondents interviewed after two calls back (N=310). (The 310 subjects interviewed represented a response rate of 86% of the original 360 household contacts.)

The Measurement of Seasonal Affective Disorder

Population estimates of seasonal affective disorder were based on the Seasonal Pattern Assessment Questionnaire developed at the National Institute of Mental Health (12, 13). Follow-up clinical interviews and independent measures of depression have provided initial validation of the use of the Seasonal Pattern Assessment Questionnaire in epidemiologic studies (10). Furthermore, prevalence estimates based on the Seasonal Pattern Assessment Questionnaire show the expected variation by latitude (6, 7, 10).

The global seasonality score used in this study was derived from six questions on the Seasonal Pattern Assessment Questionnaire regarding changes in mood (overall feeling of well-being), sleep length, social activity, weight, appetite, and energy level. Each of these items was rated on a 5-point scale on which 0=no change and 4=extremely marked change. The potential range of scores was 0 to 24. Global seasonality scores were linked with an assessment of the severity of complaints of the combined symptoms on a 5-point scale on which 1=mild and 4=disabling. These two items were used to group respondents into those with seasonal affective disorder, those with subsyndromal seasonal af-

fective disorder, and those with no seasonal affective disorder (normal subjects).

Differing threshold values for global seasonality score have been used; a global seasonality score of 10 or more has been applied in some telephone surveys, but a global seasonality score of 11 or more has been used in self-administered surveys (7). We chose the higher threshold value for our analyses, thus potentially underestimating the prevalence of seasonal affective disorder. However, prevalence estimates based on both criteria will be compared.

Measurement of General Depression

General depression was measured with the 20-item Center for Epidemiologic Studies Depression Scale (CES-D Scale) (14). This scale assesses the presence and frequency of depressive symptoms over the previous week. The CES-D Scale has been used effectively in cross-ethnic studies (15), and its validity has been demonstrated with rural populations (16). The self-administered CES-D Scale has been shown to correlate moderately well with the Hamilton Rating Scale for Depression (14).

RESULTS

Prevalence of Seasonal Affective Disorder

Table 1 reviews the criteria and resulting assignment of the subjects to diagnostic groups. Estimates based on the higher threshold (used in the self-administered tests) and the lower threshold (used in telephone surveys) are presented. Subsequent analysis will be based on groups defined by the higher global seasonality score.

As shown in table 1, 9% of the Fairbanks respondents met criteria for seasonal affective disorder and another 19% met criteria for subsyndromal seasonal affective disorder. A chi-square test of hypothesized proportions for the two classification schemes was not significant (table 1), indicating that the estimates for the two global seasonality score criteria were within the limits of random variation. The higher rates according to the lower global seasonality score value came from the category of subsyndromal seasonal affective disorder (table 1).

Individual Characteristics

Univariate comparisons of the sociodemographic characteristics of the subjects in the three diagnostic groups are given in table 2. The proportion of women in each group, although lower than that reported for clinical populations, was significantly higher in the groups of subjects with seasonal affective disorder and subsyndromal seasonal affective disorder than in the group of normal subjects.

No statistically significant differences were found for ethnicity; the prevalence of seasonal affective disorder

TABLE 1. Prevalence of Seasonal Affective Disorder in 283 Residents of Fairbanks, Alaska, According to Two Diagnostic Thresholds

Threshold ^a	Seasonal Affective Disorder			Subsyndromal Seasonal Affective Disorder			No Seasonal Affective Disorder		
	Criteria ^b	N	%	Criteria ^b	N	%	Criteria ^b	N	%
Higher threshold	Global seasonality score ≥ 11 and complaints rated ≥ 2	26	9.2	Global seasonality score ≥ 11 and complaints rated 0 or 1 or global seasonality score = 9 or 10 and complaints rated 1	54	19.1	Global severity score < 9 or global severity score = 9 or 10	203	71.7
Lower threshold	Global seasonality score ≥ 10 and complaints rated ≥ 2	28	9.9	Global seasonality score ≥ 10 and complaints rated 1 or global seasonality score = 8 or 9 and complaints rated 2	68	24.0	Global seasonality score < 8 or global seasonality score = 8 or 9 and complaints rated 1	187	66.1

^aDifferences in diagnostic assignment of patients by the two thresholds were not statistically significant ($\chi^2=5.04$, $df=2$, n.s.).

^bThe global seasonality score was derived from six questions rating sleep length, social activity, weight, appetite, and energy level on a 5-point scale on which 0=no change and 4=extremely marked change. The potential range of scores was 0 to 24. The severity of the respondent's complaints of the combined symptoms was rated a 5-point scale on which 1=mild, 2=moderate, 3=marked, 4=severe, and 5=disabling.

TABLE 2: Relation of Sociodemographic Characteristics to Seasonal Affective Disorder in 283 Residents of Fairbanks, Alaska^a

Characteristic	Subjects With Seasonal Affective Disorder (N=26)		Subjects With Subsyndromal Affective Disorder (N=54)		Normal Subjects (N=203)		Total (N=283)		χ^2 (df=2)	p
	N	%	N	%	N	%	N	%		
Sex									9.12	<0.05
Men	8	30.8	22	40.7	115	56.7	145	51.2		
Women	18	69.2	32	59.3	88	43.3	138	48.8		
Ethnicity									5.52	n.s.
White	22	84.6	43	79.6	165	81.3	230	81.3		
Black	1	3.8	7	13.0	15	7.4	23	8.1		
Alaska Native	3	11.5	3	5.6	13	6.4	19	6.7		
Education									1.59	n.s.
Less than college	22	84.6	43	79.6	159	78.3	224	79.2		
College graduate	3	11.5	9	16.7	44	21.7	56	19.8		
Employment status									7.69	n.s.
Employed full-time	9	34.6	32	59.3	111	54.7	152	53.7		
Unemployed	7	26.9	14	25.9	30	14.8	51	18.0		
Marital status									1.59	n.s.
Married or living with someone	15	57.7	29	53.7	124	61.1	168	59.4		
Other	11	42.3	25	46.3	78	38.4	114	40.3		

^aChi-square tests were based on the number of subjects for whom data on each characteristic were available. Some of the comparisons did not include all of the subjects.

was not demonstrated to differ among white, black, and Alaska Native respondents. Caution must be applied in interpreting this finding because the sizes of the nonwhite groups are small. Differences in education level, employment status, and marital status were not significant.

Consistent with earlier studies (7, 10), there was a significant difference in mean age among the three groups: the group with subsyndromal seasonal affective disorder was youngest and the group without seasonal affective disorder was the oldest. The mean age of the

subjects with seasonal affective disorder was 35.81 years ($SD=11.87$), and that of the subjects with subsyndromal seasonal affective disorder was 34.78 ($SD=9.92$). These two groups were about 6 years younger than the normal subjects, whose mean age was 42.02 ($SD=13.57$) ($F=8.41$, $df=2$, 280 , $p<0.05$).

The mean length of time the subjects had lived in Alaska also varied significantly. The subjects with seasonal affective disorder had been in Alaska for a mean of 14.81 years ($SD=8.61$), the subjects with subsyndromal seasonal affective disorder had been there for 11.96

TABLE 3. Polytomous Logistic Regression of Sociodemographic Characteristics and Diagnosis of Seasonal Affective Disorder in Fairbanks, Alaska

Comparison	Parameter	SE	χ^2 (df=2)	p	Odds Ratio
Subjects with seasonal affective disorder compared with normal subjects					
Sex ^a	1.09	0.46	5.66	0.02	2.96
Age ^b	1.04	0.49	4.59	0.03	2.84
Time lived in Alaska ^c	0.55	0.51	1.14	0.28	1.73
Ethnicity ^d	-0.38	0.70	0.29	0.59	0.69
Subjects with subsyndromal seasonal affective disorder compared with normal subjects					
Sex ^a	0.68	0.33	4.40	0.03	1.98
Age ^b	1.36	0.38	12.62	0.0004	3.88
Time lived in Alaska ^c	0.68	0.39	3.03	0.08	1.97
Ethnicity ^d	-0.39	0.68	0.33	0.57	0.68

^aFemale=1, male=0.^b<40 years=1, ≥40 years=0.^c<15 years=1, ≥15 years=0.^dAlaska Native=1, non-Alaska-Native=0.

years (SD=6.25), and the normal subjects had been there for 17.6 years (SD=11.15) ($F=6.72$, $df=2$, 280, $p<0.05$). Age and time spent in Alaska, as might be expected, were correlated ($r=0.51$, $df=282$, $p<0.01$).

Multivariate Analysis

To further investigate the observed associations between these potential predictor variables and seasonal affective disorder, a multivariate logistic regression analysis was applied to the variables involved. In addition to sex, age, and amount of time the subject had lived in Alaska, ethnicity was included in the analysis because of potential theoretical interest.

Because the subjects were classified into three diagnostic groups, polytomous logistic regression techniques were used (17). This approach yields two sets of parameters for the logits involving two comparisons of dependent variable categories. The first logit compared normal subjects and subjects with seasonal affective disorder; the second compared normal subjects and subjects with subsyndromal seasonal affective disorder. Interpretation of each set of parameter estimates and their tests of significance is the same as that for a conventional logistic regression using a dichotomous dependent variable. This approach provides estimates based on the differences among the diagnostic categories within a single analysis.

The independent variables were treated as dichotomies. Dichotomous predictor variables were used to facilitate interpretation of odds ratios (the relative odds of being in a particular diagnostic group for subjects in one predictor category compared with subjects in the other category of the same predictor variable). Treating age and the number of years the subject had lived in Alaska as continuous variables produced no substantial differences in the results of the analysis.

Table 3 shows the logistic coefficients, standard errors, and odds ratios for the four independent variables in each binary combination of categories of the depend-

ent variable. For each comparison, one value of the independent variable serves as the reference category for the other value. Only main effects are shown because no significant interactions among independent variables were detected.

In the comparison of subjects with seasonal affective disorder versus normal subjects, we found that women were 2.96 times more likely than men to be in the seasonal affective disorder group. Those under 40 years of age were 2.84 times more likely to be in the seasonal affective disorder group. The number of years the subject had lived in Alaska was not significant in this multivariate analysis, a function of its correlation with age. The univariate relation in table 2 may be considered misleading. Ethnicity does not discriminate between general depression and seasonal affective disorder.

The comparison of subjects with subsyndromal seasonal affective disorder versus normal subjects showed essentially the same pattern as the comparison of subjects with seasonal affective disorder versus normal subjects (table 3). Women were 1.98 times more likely to be in the seasonal affective disorder group, and younger subjects were 3.88 times as likely to be classified as having subsyndromal seasonal affective disorder. The effect of number of years the subjects had lived in Alaska approached significance in this comparison. Further research should examine the potential relation between subsyndromal seasonal affective disorder and length of time in a northern environment.

Further analysis comparing the subjects with seasonal affective disorder and those with subsyndromal seasonal affective disorder revealed no statistically significant differences on these sociodemographic variables. Sex and age effects were statistically equivalent for these two groups.

General Depression and Seasonal Affective Disorder

The subjects reporting symptoms consistent with a clinical diagnosis of seasonal affective disorder had a

TABLE 4. Logistic Regression of Sociodemographic Characteristics, Depression Scores on the CES-D Scale, and Diagnosis of Seasonal Affective Disorder in Residents of Fairbanks, Alaska

Comparison	Parameter	SE	χ^2 (df=2)	p	Odds Ratio
Subjects with seasonal affective disorder compared with normal subjects					
Sex ^a	1.24	0.49	6.49	0.01	3.46
Age ^b	0.85	0.51	2.75	0.10	2.33
Time lived in Alaska ^c	0.71	0.54	1.70	0.19	2.03
Ethnicity ^d	-0.50	0.73	0.47	0.49	0.60
CES-D Scale score	0.11	0.03	20.18	0.0001	1.76 ^e
Subjects with subsyndromal seasonal affective disorder compared with normal subjects					
Sex ^a	0.74	0.34	4.91	0.03	2.10
Age ^b	1.25	0.39	10.33	0.001	3.50
Time lived in Alaska ^c	0.77	0.40	3.70	0.05	2.17
Ethnicity ^d	0.38	0.69	0.29	0.59	1.46
CES-D Scale score	0.07	0.02	12.02	0.0005	1.44 ^e

^aFemale=1, male=0.^b<40 years=1, ≥40 years=0.^c<15 years=1, ≥15 years=0.^dAlaska Native=1, non-Alaska-Native=0.^eOdds ratio for each increase of 5 points in depression score.

mean CES-D Scale score of 15.08 (SD=9.75), those with subsyndromal symptoms of seasonal affective disorder had a mean score of 11.19 (SD=10.33), the normal subjects had a mean score of 6.01 (SD=6.91), and the whole group had a mean score of 7.84 (SD=8.50). The one-way analysis of variance, conducted to examine between-group differences on mean scores, indicated that the subjects reporting symptoms consistent with a clinical diagnosis of seasonal affective disorder and those with subsyndromal symptoms of seasonal affective disorder had significantly higher scores than normal subjects and the group as a whole ($F=20.22$, $df=2$, 270, $p<0.0000$) ($R=0.36$, $df=282$, $R^2=0.13$). The pattern of scores and the strength of the group differences support the assignment of members to groups according to the Seasonal Pattern Assessment Questionnaire diagnostic criteria.

The mean CES-D Scale score for the entire sample was near the lower end of the range of other reported population means, typically 8.0 to 9.3 (14). Average levels of general depression in Fairbanks during the winter are comparable to those in other communities in the United States. Although the CES-D Scale is not generally used as a diagnostic tool, scores of 16 or more may indicate clinical depression (14, 18).

Diagnoses of seasonal affective disorder and subsyndromal seasonal affective disorder have been shown to be related to sex, age, and general depression classified according to the CES-D Scale, but the question remains as to how seasonal affective disorder differs from general depression. Although the available data do not allow a definitive test of this question, we conducted an assessment of whether the risk factors of sex and age have a unique relationship to seasonal affective disorder or are related only through more general underlying depression.

Table 4 shows the results when CES-D Scale depression scores were added to the logistic regression model

developed in table 3. CES-D Scale depression scores were entered as a continuous variable, serving as a covariate or control variable, and the resulting parameters were estimated simultaneously.

In the comparison of subjects with seasonal affective disorder versus normal subjects the only notable change was that there was no longer a significant difference in the ages of the two groups with depression held constant, although the subjects with seasonal affective disorder still tended to be younger. The comparison of subjects with subsyndromal seasonal affective disorder and normal subjects did not change in any significant way. The probability for the number of years the subject had lived in Alaska parameter approached significance ($p<0.05$). This relation should receive further attention in future research. After controlling for differences in depression, subjects with seasonal affective disorder or subsyndromal seasonal affective disorder were more likely to be women and subjects with subsyndromal seasonal affective disorder were likely to be younger.

For both comparisons, subjects with seasonal affective disorder and subsyndromal seasonal affective disorder had significantly higher general depression scores, regardless of sex or age. An odds ratio for each unit of increase in general depression (here 5 points was chosen) showed the increasing likelihood that a subject would be in the seasonal affective disorder or subsyndromal seasonal affective disorder group (table 4). This estimate assumed that the relation between seasonality and affective disorder is linear; exact estimates should be interpreted with caution.

A more global interpretation of these findings is that when general depression is controlled for, age and sex are still related to seasonal affective disorder. Among women and men with the same levels of general depression, women were more likely to be diagnosed with seasonal affective disorder, and younger people were more

TABLE 5. Summary of Prevalence Estimates of Seasonal Affective Disorder in Five Areas of the United States^a

Site	Latitude	N	Seasonal Affective Disorder (%)	Subsyndromal Seasonal Affective Disorder (%)	Seasonal and/or Subsyndromal Seasonal Affective Disorder (%)
Fairbanks, Alaska (interview)	65° North	283	9.2	19.1	28.3
Nashua, N.H. (mail survey)	43° North	382	9.7	11.0	20.7
New York City (mail survey)	41° North	193	4.7	12.4	17.1
Montgomery County, Md.	39° North				
Mail survey		576	6.3	10.4	16.7
Telephone survey		383	4.3	13.5	17.8
Sarasota, Fla. (mail survey)	27° North	426	1.4	2.6	4.0

^aAccording to random sampling and measures of seasonal affective disorder based on the Seasonal Pattern Assessment Questionnaire (6, 7, 10).

at risk than older people with the same level of general depression. Further, the pattern of general depression across groups remained and was not the result of age and sex differences among respondents. Seasonal affective disorder and general depression measured by the CES-D Scale are related, but the fact that sex and age differences remained suggests that seasonal affective disorder may represent a domain somewhat distinct from depressive symptoms *per se*.

DISCUSSION

These findings indicate that more than one in four residents of Fairbanks, Alaska, may be adversely affected by the dramatic seasonal changes occurring at that latitude. Nearly one in 10 suffers symptoms severe enough to be given a diagnosis of seasonal affective disorder.

Table 5 summarizes prevalence estimates from this and comparable studies (6, 7, 10) using random sampling and measures of seasonal affective disorder based on the Seasonal Pattern Assessment Questionnaire. The estimates for seasonal affective disorder and subsyndromal seasonal affective disorder are ordered by the latitude at which the study took place. The estimated prevalence of seasonal affective disorder for Fairbanks was higher than estimates for all areas reported except Nashua, N.H. However, when a global seasonality score value of 10 rather than 11 was used to define seasonal affective disorder, the prevalence estimate for Fairbanks became 9.9% (table 1), surpassing Nashua. Fairbanks had the highest figure for subsyndromal seasonal affective disorder and for the combination of seasonal affective disorder and/or subsyndromal seasonal affective disorder. These seven studies generally support the widely held hypothesis that the prevalence of seasonal affective disorder increases with latitude and the corresponding extreme seasonal shifts in available daylight. Therefore, phototherapy, a unique treatment for seasonal affective disorder, may have widespread clinical application during the winter season in the far north.

In the current study, only age and sex were demonstrated to be associated with the occurrence of seasonal affective disorder (table 3). Younger people of both sexes were more likely to have seasonal depressive symptoms and were more likely to be diagnosed with

seasonal affective disorder. Both older and younger women were more likely to experience seasonal affective disorder. These risk factors remained significant when differences in general depression were controlled for (table 4). These findings in a community population are similar to those for clinical populations in which early onset and a high predominance of women have been found (3).

General depression was associated with seasonal affective disorder in this study. The subjects with seasonal affective disorder had significantly higher CES-D Scale scores than normal subjects and subjects with subsyndromal seasonal affective disorder, and subjects with subsyndromal seasonal affective disorder had significantly higher CES-D Scale scores than normal subjects. The relation between general depression and seasonal affective disorder persisted, even when age and sex differences were controlled for (table 4). The Seasonal Pattern Assessment Questionnaire appears to be sensitive to general depression while differentiating seasonal affective disorder on the basis of age and sex.

The small number of Alaska Natives limits the opportunity to test for the potential effects of differences in race/ethnicity, especially between Alaska Natives and non-Alaska-Natives. Moreover, all Alaska Natives in this sample were residing in an urban environment, preventing the exploration of potential mediating influences of differences in life style. Adaptation to a northern environment remains an important issue for future studies.

This study supports the conclusions that seasonal affective disorder is a depressive disorder that is prevalent in northern populations and that sex and age may represent the major risk factors that differentiate it from the general experience of depression in those communities. Further research to define populations at risk and to identify factors associated with treatment outcome may improve the well-being and productivity of those affected by seasonal affective disorder and its subsyndromal manifestations.

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Duration of Psychosis and Outcome in First-Episode Schizophrenia

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Objective: This study was undertaken to assess the potential effect of duration of untreated illness on outcome in a group of first-episode schizophrenic patients. **Method:** Seventy patients with schizophrenia diagnosed according to the Research Diagnostic Criteria entered the study and were followed for up to 3 years. All patients received standardized treatment and uniform assessments both during the acute phase of their illness and throughout the follow-up period. Outcome was measured in terms of time to remission of acute psychotic symptoms as well as degree of symptom remission. **Results:** The mean duration of psychotic symptoms before initial treatment was 52 weeks, preceded by a substantial prepsychotic period. According to survival analysis, duration of illness before treatment was found to be significantly associated with time to remission as well as with level of remission. The effect of duration of illness on outcome remained significant when diagnosis and gender variables, themselves associated with outcome, were controlled in a regression analysis. Duration of illness was not correlated with age at onset, mode of onset, premorbid adjustment, or severity of illness at entry into the study. **Conclusions:** Duration of psychosis before treatment may be an important predictor of outcome in first-episode schizophrenia. Acute psychotic symptoms could reflect an active morbid process which, if not ameliorated by neuroleptic drug treatment, may result in lasting morbidity. Further implications of these findings are discussed.

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Considerable attention has been focused on clinical factors that may influence the outcome of patients with schizophrenia. These have included premorbid factors such as the patient's level of social and educational functioning, age at onset of illness, mode of onset of illness, diagnosis, and gender. Poor premorbid adjustment, early and gradual mode of onset, the absence of affective features, and male gender have all been associated with poorer outcome. These findings have contributed to the notion that factors inherent in a patient's illness determine outcome (1).

At the same time, several investigators have described

the potential impact on outcome of duration of untreated illness, i.e., the time interval between symptom onset and institution of neuroleptic treatment (2-9). Crow et al. (2) reported that among 120 patients in their first episode of schizophrenia who were followed for 2 years in a randomized, placebo-controlled trial of maintenance neuroleptic treatment, relapse subsequent to initial hospital discharge was substantially more common in those whose pretreatment illness lasted more than 1 year. Relapse rates in this group were high: only 18% of the patients who were given active treatment and none who were given placebo remained free of relapse after 2 years. May et al. (3-5) randomly assigned 228 first-admission schizophrenic patients to five treatment groups, three of which did not include drug treatment (psychotherapy, milieu therapy, and ECT groups) and two of which did (drug alone and drug plus psychotherapy). Patients from the first three groups who did not respond were subsequently treated with antipsychotic drugs. In this investigation the drug-treated groups showed the best response and, together with the ECT group, showed the best outcome for up to 3 years (as measured by clinical, social, and psychological test criteria). Thus, the groups initially not treated with medication were found to have a poorer

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outcome over the follow-up period, despite the fact that subsequent treatment after the index admission was similar (although not standardized) among all groups. Wyatt (6, 7) has recently shown, in a new analysis of these data, that following discharge, patients who had not been treated with neuroleptics and who were discharged within 6 months of initial hospitalization required significantly more rehospitalization and as much subsequent neuroleptic treatment as patients who had initially received neuroleptics. Thus, even patients who initially responded well to nonneuroleptic treatment subsequently fared worse than patients who were initially treated with neuroleptics.

Further evidence for the finding that early neuroleptic treatment can enhance treatment response and outcome in schizophrenia may be derived from early studies on antipsychotic drug use (6, 8). Angrist and Schulz (8) reviewed 10 of these investigations (performed in the 1950s) that studied both acute and chronic patients who had not previously received drug treatment. Poorer response to neuroleptics was found among the chronic patients in six studies, suggesting that delay in drug treatment may lead to a significantly worse outcome.

Lo and Lo (9), in a retrospective 10-year follow-up study of 133 Chinese schizophrenic patients aged 14 to 60 years, found that shorter duration of untreated illness prior to the initial acute episode was significantly associated with favorable outcome ($p < 0.01$). Inoue et al. (10), in a retrospective evaluation of 19 treated adolescent schizophrenic and schizophreniform patients, noted that the time interval between onset of illness and first outpatient treatment varied from 1 to 6 years. Less favorable outcome—specifically, poor occupational or scholastic achievement at 3-year follow-up—was predicted by longer duration of illness (4 years or more). Rabiner et al. (11) studied a group of 64 first-episode subjects with varied diagnoses and found that the 36 schizophrenic patients had a mean duration of illness (from first signs of behavioral changes to baseline interview) of 14.5 months. This study also found that the longer the duration of illness, the poorer the outcome, as measured by presence (or absence) of remission or relapse over a 1-year follow-up period.

The question of whether the duration of psychotic symptoms prior to treatment affects the subsequent course and outcome of schizophrenia has important implications for the nature of both schizophrenic pathophysiology and treatment strategies. Previous studies have generally been retrospective, have involved diagnostically heterogeneous patient groups, and/or have not standardized both acute and maintenance treatment and follow-up. To explore the prognostic significance of the duration of acute symptoms prior to treatment, we examined the relation between outcome and various clinical factors, including premorbid adjustment, age at onset, mode of onset, diagnosis, gender, and duration of illness prior to treatment, in a group of first-episode psychotic patients. Patients were followed for up to 3 years with the use of a standardized treatment protocol and follow-up assessments.

METHOD

Subjects in this study were drawn from a larger, ongoing prospective study of psychobiology in first-episode schizophrenia, the design and procedures of which have been previously described (12). In summary, the subjects were hospital inpatients, all of whom were in the acute phase of their first psychotic episode, necessitating hospital admission, who met the Research Diagnostic Criteria (RDC) (13) for schizophrenia or schizoaffective disorder, mainly schizophrenic. The subjects had not received more than 12 weeks of neuroleptic treatment in their lifetime; 70% of the group had never received any neuroleptic. If patients had received medications before admission, these were withdrawn at least 14 days before the baseline evaluations. No subject had a past history of significant neurological or endocrine disorder or persistent or severe substance abuse. All patients, as well as their families, were advised of the study and gave written informed consent.

Psychopathology at baseline was evaluated with the following measures: the Schedule for Affective Disorders and Schizophrenia (SADS) (14), the Scale for the Assessment of Negative Symptoms (15), and the Clinical Global Impression (CGI) scale (16). During their initial hospital admission, patients' premorbid status was investigated with the Premorbid Adjustment Scale (17), and age at onset and mode of onset of illness were ascertained by interviews with the patients and family members. Multiple informants were available and were used to obtain these data for all study subjects. Onset of illness was determined in two ways. First, we asked patients and their family members when the patient (or the family member) first experienced (or noticed) behavioral changes which, in retrospect, appear to have been related to the patient's becoming ill. Second, after explaining psychosis in clear language, we asked when the patient (or the family member) first experienced (or noticed) psychotic symptoms. When differences between patients' and family members' responses occurred, a consensus decision was made by the research staff. All of these evaluations were made by staff members who were blind to patients' treatment response and outcome.

After completion of baseline procedures, patients received open standardized treatment following the study treatment algorithm (12). This consisted of an initial trial of fluphenazine, 20 mg/day p.o., for 6 weeks. If patients were clinically nonresponsive (as determined by lack of significant improvement in positive symptoms and/or presence of residual psychotic symptoms), the fluphenazine dose was increased to 40 mg/day p.o. for 4 weeks. At this point, clinical nonresponders received a 6-week trial of haloperidol, 20 mg/day p.o., followed by an increase to 40 mg/day p.o. for a further 4 weeks, as indicated. Patients with continuing poor clinical response were then given a third neuroleptic trial with a drug from a different biochemical class (molindone), for up to 6 weeks, in moderate to high dose ranges. Adjunctive treatment with lithium was given at

the end of either the haloperidol or the molindone trial. Finally, treatment-resistant patients were considered for clozapine treatment. Patients who relapsed subsequent to initial hospitalization were treated with the same medication and dose to which they had first responded. If necessary, depending on clinical response, they then received further treatment according to the treatment algorithm.

Patients were evaluated biweekly during acute treatment and monthly during the maintenance phase on the SADS (Change Version; SADS-C) with added items from a Psychosis and Disorganization Scale, the Scale for the Assessment of Negative Symptoms, and the CGI. Remission was defined as ratings of 3 or lower on the SADS-C and Psychosis and Disorganization Scale psychosis items, a CGI severity item rating of mild or less, and a rating of at least much improved on the CGI improvement item. Furthermore, this level of response was required to persist for at least 8 weeks (four consecutive biweekly ratings).

Statistical analysis included chi-square tests with Yates' correction for categorical data and Student's *t* tests for continuous data. Pearson's correlation coefficients were calculated to assess the effects of pretreatment variables on degree of remission. Survival analysis according to the Cox proportional hazards model (18) was used to test for effects of diagnosis, gender, and duration of illness on outcome. The Cox model allows for a more sensitive measure of outcome than simply presence or absence of treatment response by focusing on the time to remission (or treatment status at study endpoint). This model also enables consideration of the impact of several simultaneously entered variables on time to treatment response.

RESULTS

Analyses were performed on the data of 70 patients who met the inclusion criteria and were followed for a minimum of 8 weeks in the study. Fifty-six percent (*N*=39) of the patients were male. The mean age at entry into the study was 24.3 years (*SD*=6.0). Seventy-seven percent (*N*=54) of the patients met the RDC for schizophrenia and 23% (*N*=16) for schizoaffective disorder. Of the 70 study subjects, 44% were Caucasian, 32% were black, 17% were Hispanic, and 7% were Asian. According to Hollingshead and Redlich's Two-Factor Index of Social Position (19), 10% were from class I (upper), 19% from class II (upper middle), 28% from class III (middle), 13% from class IV (lower middle), and 28% from class V (lower). Nineteen percent of the group were high school graduates only, and 61% had at least some college education. Eighty percent of the group had never married, 10% were married, and 10% were separated or divorced. All of the patients were actively psychotic, with ratings of at least 4 on one or more of the SADS-C and Psychosis and Disorganization Scale psychosis items and at least 4 (moderately ill) on the CGI severity item.

The mean age at onset of psychotic symptoms was 23.3 years (*SD*=5.9). Duration of illness was defined in two ways: the time interval from onset of unusual behavioral or prodromal (psychiatric) symptoms to study entry and from onset of psychotic symptoms to study entry. The mean duration of illness from the onset of psychiatric symptoms was 150.8 weeks (*SD*=176.6), and the duration from the onset of psychotic symptoms was 51.9 weeks (*SD*=82.3). Duration of illness before treatment was not significantly different for the schizophrenic and schizoaffective subjects: the mean duration since onset of psychiatric symptoms was 155.1 weeks (*SD*=170.3) for the schizophrenic patients and 136.6 weeks (*SD*=201.3) for the schizoaffective patients; the mean duration since the onset of psychotic symptoms was 56.6 weeks (*SD*=89.0) for the schizophrenic patients and 35.9 weeks (*SD*=53.2) for the schizoaffective patients. Duration of psychotic symptoms for male subjects (mean=69.7 weeks, *SD*=104.3) was significantly longer than for female subjects (mean=29.4 weeks, *SD*=29.2) (*t*=2.3, *df*=45, *p*<0.03). Mode of onset was defined in terms of the time interval between the onset of psychiatric (prodromal) symptoms and the onset of psychotic symptoms. This time interval lasted a mean of 98.5 weeks (*SD*=156.6) for the whole study group. The mode-of-onset time interval was not significantly different for the schizophrenic and schizoaffective subjects, nor was there a gender difference. Male subjects were consistently younger at the onset of psychotic symptoms (mean age=22.4 years, *SD*=5.9, versus 24.3 years, *SD*=5.9, for the females) and at entry into the study (mean=23.8 years, *SD*=6.1, versus 24.9 years, *SD*=5.9, for the females). They also had a longer duration of illness since onset of any prodromal symptoms (mean=165.5 weeks, *SD*=155.6, versus 131.7 weeks, *SD*=201.8, for the females). However, these gender differences were not statistically significant.

According to the Cox proportional hazards model of survival analysis, duration of illness from onset of psychotic symptoms was a significant predictor of time to treatment response ($\chi^2=4.52$, *df*=1, *p*<0.03), with longer pretreatment symptom duration being associated with longer time to remission (table 1). This relationship was only slightly affected by a logarithmic transformation of the illness duration variable, indicating that the effect of outliers (patients with extremely long illness) on this finding was minimal. There was a trend for duration of psychotic symptoms to be associated with diagnosis as well as with gender. To control for diagnosis and gender, an analysis was done in which diagnosis, gender, and duration of illness were entered simultaneously into the Cox regression model. Duration of psychotic symptoms before treatment remained significantly associated with time to remission ($\chi^2=4.38$, *df*=1, *p*<0.04), whereas diagnosis and gender did not. Mode of onset was not associated with time to remission.

To examine the relation of pretreatment variables to outcome in another way, patients were classified (at the endpoints of their participation in the study) as in full

TABLE 1. Results of Individual Cox Regression Analyses for Associations Between Pretreatment Variables and Time to Remission in 70 First-Episode Schizophrenic Patients

Pretreatment Variable	Cox Regression Coefficient ^a	Analysis	
		χ^2 (df=1)	p
Duration of psychotic symptoms	-0.005	4.52	0.03
Duration of psychiatric (prodromal) symptoms	-0.0014	2.24	0.13
Mode of onset ^b	-0.0003	0.10	0.76
Age at onset of psychotic symptoms	0.026	1.70	0.19
Age at study entry	0.013	0.42	0.52
Premorbid adjustment			
Childhood	-0.12	0.72	0.40
Early adolescence	-0.24	2.23	0.14
Late adolescence	-0.17	2.24	0.13
Adulthood	0.09	0.63	0.43

^aEstimates the increase in "risk" of remission for each unit increase in the pretreatment variable.

^bInterval between onset of prodromal symptoms and onset of psychotic symptoms.

remission (complete response to treatment with no residual symptoms; 74%, N=49), partial remission (substantial improvement in positive symptoms but with some remaining residual positive or negative symptoms; 12%, N=8), and no remission (continued active positive symptoms; 14%, N=9) after the initial episode. Duration of illness since onset of psychiatric (prodromal) symptoms and duration of illness since onset of psychotic symptoms were correlated significantly with this measure of outcome (table 2). The mode-of-onset variable was not significantly associated with level of remission.

Earlier age at onset of psychotic symptoms was not significantly related to time to remission but was significantly associated with level of remission ($r=-0.25$, $df=64$, $p<0.05$), with younger age predicting poorer outcome. To determine whether premorbid differences among patients accounted for any variation in illness duration and outcome, premorbid adjustment (according to the Premorbid Adjustment Scale) was determined during childhood, early adolescence (ages 12–15), late adolescence (ages 16–18), and adulthood. Scale scores range from 0 (no impairment) to 6 (severe impairment) for each item. Mean Premorbid Adjustment Scale scores for the group were as follows: childhood, 1.3 (SD=0.9); early adolescence, 1.4 (SD=0.9); late adolescence, 1.7 (SD=1.2); adulthood, 1.8 (SD=1.4). Mean premorbid adjustment scores were not significantly associated with age at onset, mode of onset, or duration of illness since either psychiatric or psychotic symptoms began. Poorer premorbid adjustment levels during early and late adolescence were significantly correlated with a lower level of remission (table 2). This pattern was repeated with regard to time to remission, although these relationships did not reach statistical significance (table 1).

Duration of illness was also not correlated with age at onset, mode of onset, or severity of illness at study

TABLE 2. Correlations of Pretreatment Variables With Level of Remission in First-Episode Schizophrenic Patients

Pretreatment Variable	N	Analysis	
		Pearson's r	p
Duration of psychotic symptoms	65	0.30	0.01
Duration of psychiatric (prodromal) symptoms	66	0.43	0.0001
Mode of onset ^a	65	0.09	0.50
Age at onset of psychotic symptoms	66	-0.25	0.05
Age at study entry	66	-0.12	0.32
Premorbid adjustment			
Childhood	65	0.21	0.10
Early adolescence	64	0.27	0.03
Late adolescence	58	0.28	0.03
Adulthood	48	0.08	0.60

^aInterval between onset of prodromal symptoms and onset of psychotic symptoms.

entry. In addition, baseline severity of illness was not independently associated with outcome, as measured by either time to treatment response or level of remission.

DISCUSSION

The results of this study indicate that duration of illness prior to treatment, particularly following the onset of psychotic symptoms, may be an important predictor of outcome in first-episode schizophrenic and schizoaffective patients. Duration of psychotic symptoms before treatment was significantly associated with both time to remission and level of remission (complete, partial, or none), with longer duration predicting greater time to remission as well as a lesser degree of remission. Longer duration of illness since onset of any prodromal symptoms was also associated with poorer treatment response (degree of remission). These findings have not, to our knowledge, been previously demonstrated in a well-defined, new-onset study population followed prospectively with uniform follow-up assessments and a standardized treatment protocol.

These results support and extend the findings of the relatively few previous investigations of the impact of duration of untreated schizophrenia (2–9). In contrast, Kolakowska et al. (20) found that outcome in their group of 77 schizophrenic and schizoaffective patients was not related to duration of illness. However, this was a relatively heterogeneous group of both acute and chronic patients studied 2–20 years since the onset of their illness. We caution that outcome in the present study was measured in terms of time to treatment response, as well as level of remission, and not in terms of relapse frequency or social and occupational functioning, all of which are potentially important factors in assessing outcome (11, 21).

The gender difference in duration of illness (more than twice as long for males as for females) that we found in this study suggests that this variable could have a particularly important prognostic significance

for male first-episode schizophrenic and schizoaffective disorder patients.

Consistent with most previous studies (11, 20, 22–24), early age at onset was found to be an unfavorable prognostic feature. On the other hand, mode of onset (measured as the time interval between onset of any prodromal symptoms and onset of psychotic symptoms) did not have any prognostic significance in this study. However, the finding of a typically prolonged mode of onset in our first-episode subjects—almost twice the mean duration of frank psychotic symptoms—was unexpected and provides further evidence for the presence of a substantial prepsychotic prodromal period before the first episode of schizophrenia (10, 25). Further characterization of these prodromal symptoms, as well as their potential patterns of evolution, may be clinically important (26).

Other factors that were not specifically investigated in the present study, but which could account for the apparent relation between duration of acute symptoms and outcome, must be considered. Surprisingly, the mean duration of illness was 52 weeks since the onset of psychotic symptoms and 151 weeks since the onset of any prodromal symptoms. These findings suggest that patients can exist in the community for extended periods with substantial levels of psychopathology. Although predominantly disease-specific factors may determine the onset of illness, many sociocultural and psychosocial factors can determine when and how the patient is brought for evaluation and treatment. For example, less educated families may tolerate psychopathology to a greater extent and may seek medical attention for patients only when their symptoms become severe and/or socially disruptive. In addition, a gradual or insidious mode of onset may be associated with less severe or disruptive symptoms that do not attract attention or necessitate intervention.

Factors related to age at onset, diagnosis, and gender can similarly account for delay in seeking and obtaining treatment. In the present study, male gender was associated with a significantly longer duration of psychotic symptoms prior to treatment. Age at onset and diagnosis were not significantly associated with length of illness before treatment. However, there may presumably be greater tolerance in families and the community for deviant behavior among adolescents than among adults, enabling patients who become ill earlier to remain symptomatic longer before receiving treatment. Patients whose psychopathology has affective components may have more florid symptoms, which attract attention and result in earlier intervention. MacMillan et al. (27) found some association between higher levels of emotional arousal in the family environment and longer duration of illness before hospital admission in a sample of first-episode schizophrenic patients. This finding, as interpreted by Mintz et al. (28), suggests that expressed emotion may play a mediating role in the outcome of patients with longer illness. Duration of illness may also be a function of insight, with many patients lacking insight into their illness and thus postponing seeking treatment.

The finding that outcome may be affected by duration of acute symptoms prior to treatment suggests a role for at least some illness-related factors in schizophrenia. Although speculative, these findings suggest that an active morbid process might occur during periods of acute symptoms or decompensation which, if not ameliorated by neuroleptic drug treatment, may result in lasting morbidity. It is possible that an extended period of dopaminergic neural dysfunction may result in a more severe, or less reversible, pathophysiologic condition. Support for this hypothesis may be gained from preclinical studies of chronic treatment with dopamine agonists and antagonists, which have been shown to alter dopaminergic neural function on a persisting basis (29). These studies have demonstrated enduring behavioral and neurophysiologic effects in animal models, attributed to mechanisms of sensitization, neurotoxicity, and oxidative stress (30, 31).

Crow et al. (2) have raised the question of whether extended duration of illness is more likely to occur in illnesses that have a poor prognosis in any case or because improved outcome is related to earlier institution of treatment; that is, is there a causative relation between longer duration of illness and poorer outcome? Support for the effect of pretreatment length of illness on outcome was provided by the results of this study, since duration of psychotic symptoms prior to treatment was the only variable in the Cox regression model that was significantly associated with time to remission. In addition, duration of illness was positively correlated with another outcome measure, level (or degree) of remission. Premorbid adjustment, age at onset, mode of onset, and severity of illness at presentation were not associated with length of illness, suggesting that this variable is not simply a marker for other illness features which could account for the outcome variance.

These findings suggest that duration of illness prior to initial treatment should be included, as a potentially important predictive variable, in studies concerned with the outcome of schizophrenia. Since earlier neuroleptic treatment appears to be associated with more favorable outcome in first-episode schizophrenia, these results provide support for the clinical value of efforts directed at shortening the length of untreated illness in patients with new onset of schizophrenia (6, 32, 33).

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Cigarette Smoking in Schizophrenia: Relationship to Psychopathology and Medication Side Effects

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Objective: The authors' goal was to study the relationship between smoking status and clinical characteristics in schizophrenic patients. **Method:** Seventy-eight schizophrenic outpatients were assessed by a single rater using the Brief Psychiatric Rating Scale (BPRS), the Abnormal Involuntary Movement Scale, and the Simpson-Angus Scale for extrapyramidal symptoms. Current smokers (N=58) were compared with nonsmokers (N=20) on clinical variables by independent t tests and chi-square tests. Differences in outcome variables were tested by multiple analysis of covariance (ANCOVA) with smoking status and gender as factors and age, neuroleptic dose, and caffeine consumption as covariates. **Results:** Seventy-four percent of patients were current smokers and reported a mean of 19 cigarettes smoked per day. Compared to nonsmokers, current smokers were significantly more likely to be men, to be younger, and to have had an earlier age at onset and a greater number of previous hospitalizations. Current smokers and nonsmokers received mean neuroleptic doses of 1160 and 542 mg/day (chlorpromazine equivalents); the difference was significant. Current smokers also displayed significantly less parkinsonism and more akathisia and had higher total scores on the BPRS. Overall multiple ANCOVA demonstrated a significant main effect for smoking status but not gender or the interaction between gender and smoking status. Univariate ANCOVAs demonstrated a significant main effect of smoking status only for the Simpson-Angus Scale score. **Conclusions:** Cigarette smokers receive significantly higher neuroleptic doses, in part because of a smoking-induced increase in neuroleptic metabolism. Smoking is also associated with significant reduction in levels of parkinsonism. Smoking status is a significant factor that should be considered in assessment of neuroleptic dose requirements and neuroleptic side effects.

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It is readily apparent to clinicians working with chronic schizophrenic patients that this population is prone to cigarette smoking, often smoking quite heavily. Surveys of schizophrenic patients have demonstrated rates of smoking between 74% and 92%, compared to 35%-54% for all psychiatric patients and 30%-35% for the general population (1-3). Schizophrenic patients smoke at a significantly higher rate than other psychiatric patients even when contributing factors such as marital status, alcohol use, and socioeconomic status are controlled (2). Given the serious health risks associated with smoking, the question of why these patients smoke so heavily is of considerable importance. In addition, as psychiatric inpatient units increasingly adopt no smoking policies, the impact of

cigarette smoking and abstinence requires greater clarification in this patient population.

It has been suggested that the high rate of smoking among schizophrenic patients might reflect the effects of institutionalization, boredom, and poor impulse control (2, 4, 5). Gopaldaswamy and Morgan (1) suggested that smoking is one of the few pleasures available to many schizophrenic patients. These authors also speculated that cigarette smoking might improve underlying psychopathology by enhancing concentration and reducing discomfort from hyperarousal. In their survey of 59 schizophrenic patients, Glynn and Sussman (6) noted that smoking produced relaxation and reduced anxiety in most respondents. Twenty percent of schizophrenic smokers reported that smoking reduced medication side effects, and an equal number reported smoking in response to psychiatric symptoms.

Cigarette smoking may decrease antipsychotic side effects through a pharmacokinetic interaction. Three groups have demonstrated increased clearance of neuroleptics associated with cigarette smoking, ranging from 44% to 67% for orally administered haloperidol

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and fluphenazine (7, 8) and 133% for fluphenazine decanoate (8). Most surveys have found a correspondingly higher mean neuroleptic daily dose administered to smokers than to nonsmokers (9–11). Swett and colleagues (5) demonstrated lower levels of chlorpromazine-induced sedation in smokers, which they attributed to lower chlorpromazine plasma concentrations. Similarly, Stimmel and Falloon (12) demonstrated changes in chlorpromazine plasma concentrations and side effects in a schizophrenic patient who stopped and subsequently resumed smoking.

Cigarette smoking might also affect schizophrenic symptoms and antipsychotic actions through the modulation of dopamine activity. Nicotinic acetylcholine receptors have been identified on mesolimbic and nigrostriatal dopaminergic neurons (13). In rats, acute administration of nicotine stimulates release of dopamine in the striatum and nucleus accumbens by acting on presynaptic nicotine receptors (14). Nicotine also acutely elevates levels of the enzyme tyrosine hydroxylase in the nucleus accumbens, indicating enhanced dopamine turnover (15). Some evidence suggests that the stimulatory effect of anticholinergic agents on dopaminergic activity may result in part from an increase in acetylcholine acting on nicotinic receptors (16).

Several studies in the general population have associated cigarette smoking with a significant reduction in the incidence of idiopathic Parkinson's disease (17–21). This may represent a protective effect of cigarette smoking, since smoking behaviors start decades before the onset of parkinsonism. Nicotine has been used in the treatment of postencephalitic parkinsonism (22). While cigarette smoking can produce tremor in normal subjects, tremor is reduced in patients with parkinsonism (23). The relationship between cigarette smoking and neuroleptic-induced parkinsonism is less clear. In a study of 130 psychiatric inpatients, Decina et al. (9) found significantly less parkinsonism in smokers than in nonsmokers, while Wagner et al. (24) found this effect only in schizophrenic patients with a duration of illness less than 7 years. Yassa and co-workers (11) did not find a relationship between cigarette smoking and parkinsonism, but only 11 patients with parkinsonism were identified in their sample of 154 chronic psychiatric patients. In addition, two studies have found increased tardive dyskinesia in smokers versus nonsmokers (11, 25).

Finally, it has also been suggested that patients with schizophrenia may smoke to medicate underlying symptoms of their illness. Two surveys have demonstrated a greater rate of smoking among persons with prior depressive episodes (26, 27). This finding may reflect a specific reinforcing property of nicotine's mood-elevating effect (28). Nicotine also has been reported to cause calming and alerting effects (29–32). In normal subjects, nicotine improves vigilance and efficiency of information processing and may improve learning (33, 34). The effects of nicotine on schizophrenic symptoms and cognition have not been studied directly.

To further characterize factors associated with ciga-

rette smoking in chronic schizophrenic patients, we assessed clinical symptoms and medication side effects in relationship to smoking status and smoking history.

METHOD

The study was conducted in the outpatient clinic of an urban mental health center. All patients with a diagnosis of schizophrenia were invited to participate. Diagnoses were verified by a research psychiatrist using the Structured Clinical Interview for DSM-III-R (SCID) (35). Patients were assessed by a single rater using the Brief Psychiatric Rating Scale (BPRS) (36), the modified Simpson-Angus Scale for extrapyramidal symptoms (37), and the Assessment for Involuntary Movement Scale (AIMS) (38). After completion of these rating scales, a semistructured interview was conducted to obtain information about the chronology of the patient's illness, treatments, and smoking history. Whenever possible, the patient's history was corroborated by the medical record, clinicians, and family members. The average daily intake of all caffeinated beverages was calculated and recorded as cups of coffee consumed per day. Patients were considered current smokers if they reported smoking a minimum of five cigarettes daily over the past 6 months. Former smokers had smoked at this level during a previous 6-month period, and nonsmokers had never smoked at this level.

Baseline comparisons between smokers and nonsmokers were made by using independent *t* tests for continuous variables and chi-square tests for categorical variables. The cohort was restricted to patients receiving neuroleptic treatment for comparisons of medication side effects (Simpson-Angus Scale, akathisia, AIMS). We performed 2×2 multiple analyses of covariance (ANCOVAs) (with gender and smoking as factors and age, caffeine intake, and neuroleptic dose as covariates) using BPRS total score, positive and negative symptoms subscales, Simpson-Angus Scale total score, akathisia score, and AIMS total score as dependent variables. Where overall multiple ANCOVA main effects were significant, univariate ANCOVAs were performed on that main effect. Results are reported for all comparisons that were tested. Former smokers are combined with nonsmokers for comparisons unless otherwise stated.

RESULTS

Eighty-five patients were asked to participate, and 79 consented. One respondent, an exclusive pipe smoker who claimed that he did not inhale, was dropped from the study. Fifty-nine (76%) of the 78 participants were men and 19 (24%) were women. The mean age was 43 years (*SD*=9.5) (range=23–64), and mean duration of illness was 17.7 years (*SD*=8.9) (range=2–40). Seventy-two patients were receiving antipsychotic medication at a mean daily dose of 989 mg (*SD*=963) of chlorproma-

TABLE 1. Characteristics of Smoking and Nonsmoking Schizophrenic Patients^a

Item	Smokers (N=58)		Nonsmokers ^b (N=20)		Analysis		
	Mean	SD	Mean	SD	t	df	p
Age (years)	40.5	8.2	49.2	10.5	3.8	76	0.0003
Age at onset (years)	23.2	6.9	30.1	11.1	3.2	76	0.002
Number of hospitalizations	7.4	6.2	4.5	3.5	2.0	75	0.05
Coffee intake (cups/day)	6.7	4.3	4.6	3.4	2.1	76	0.04
BPRS total score	34.4	8.3	29.1	8.8	2.4	76	0.02
Positive symptoms	8.5	3.9	6.1	3.7	2.4	76	0.02
Negative symptoms	6.2	2.2	5.1	2.0	2.2	76	0.03
Depression	8.5	3.3	8.1	3.5	0.5	76	0.60
Tension	2.1	0.6	2.2	1.0	0.3	76	0.70
Excitement	1.1	0.4	1.0	0.0	1.6	76	0.10
Neuroleptic dose ^c (chlorpromazine equivalents, mg/day)	1160	956	542	849	2.5	70	0.01
Modified Simpson-Angus Scale for							
Extrapyramidal Symptoms score	0.6	0.9	1.6	2.5	2.5	70	0.01
Akathisia score	1.2	0.8	0.8	0.9	2.5	70	0.03
AIMS total score	3.8	2.6	5.1	3.2	1.7	70	0.10

^aNine smokers (16%) and 10 nonsmokers (50%) were women ($\chi^2=7.8$, $df=1$, $p=0.005$).

^bIncludes former smokers.

^cN=72.

zine equivalents (range=35–3700). Fifty-eight (74%) were current smokers, 11 (14%) were nonsmokers, and nine (12%) were former smokers. Nine (16%) of the current smokers started smoking after the onset of their psychiatric illness. The 58 current smokers reported smoking an average of 28.9 cigarettes per day ($SD=14.7$) and had started smoking at a mean age of 16.7 years ($SD=6.7$).

Current smokers were compared with nonsmokers (former smokers and those who had never smoked) on demographic and clinical variables (table 1). Current smokers were significantly more likely to be male: 49 (84%) were men, compared with 10 (50%) of the nonsmokers ($\chi^2=7.8$, $df=1$, $p=0.005$). Current smokers were also younger, had an earlier age at onset and a greater number of prior hospitalizations, and reported drinking more caffeine per day. Only one subject from each of the two groups acknowledged current or past alcohol abuse, and only two subjects from the current smokers group acknowledged abuse of other substances (both marijuana).

Current smokers scored significantly higher on the BPRS than nonsmokers (table 1). Analysis of subscales of the BPRS (39, 40) revealed current smokers to have higher levels of both positive and negative symptoms. Current smokers did not differ significantly in levels of depression, tension, or excitement as measured by the BPRS.

The seventy-two patients currently receiving antipsychotic medication were compared according to measures of medication side effects. Current smokers were receiving a significantly higher dose of neuroleptic than were nonsmokers (1160 mg/day versus 542 mg/day of chlorpromazine equivalents). The two groups did not differ in mean weight or in the frequency of concurrently prescribed anticholinergic medication. Current smokers displayed significantly less parkinsonism and more akathisia as measured by the Simpson-Angus

Scale. There was a trend for current smokers to exhibit less tardive dyskinesia ($p=0.10$) as measured by the total score on the first eight items of the AIMS.

Overall multiple ANCOVA showed a significant main effect for smoking status ($F=2.44$, $df=5$, 61, $p=0.04$) but not for gender ($F=1.93$, $df=5$, 61, $p=0.11$) or the interaction between gender and smoking status ($F=0.36$, $df=5$, 61, $p=0.87$). Since no significant Gender by Smoking Status interaction effects were found for any dependent variable, main effects could be assessed unambiguously (table 2). A significant main effect of smoking status was found for the Simpson-Angus Scale total score but not for scores on the BPRS total score, positive and negative subscales, akathisia, or AIMS. Of the covariates, caffeine intake was significantly related to the total BPRS score and the positive symptoms subscale but was not related to the negative symptoms subscale, Simpson-Angus Scale, akathisia, or AIMS. Neuroleptic dose was related to the negative symptoms subscale of the BPRS but not to any of the other outcome measures.

DISCUSSION

Our results are consistent with other studies that report high rates of cigarette smoking in schizophrenic patients; the men in our sample smoked at a higher rate than the women (83% versus 47%). Smokers in our sample were prescribed neuroleptic at roughly twice the daily dose prescribed for nonsmokers. This finding is in keeping with the smoking-induced elevation of hepatic clearance of neuroleptic drugs previously described (7, 8, 41). Lacking measures of plasma concentrations of neuroleptics in our two patient groups, we can only infer that neuroleptic activity levels in smokers were comparable to, and perhaps higher than, levels in nonsmokers on the basis of the higher mean level of akathisia

TABLE 2. Univariate Analyses of Variance in Psychopathology Among Smoking and Nonsmoking Schizophrenic Patients

Dependent Variables	F Ratio				
	Factors		Covariates		
	Cigarette Smoking	Gender	Caffeine Intake	Age	Neuroleptic Dose
BPRS total score	1.7	0.05	4.7 ^a	0.4	1.7
Positive symptoms	2.6	0.1	5.4 ^a	0.02	1.0
Negative symptoms	1.1	3.6	0.002	0.003	4.6 ^a
Modified Simpson-Angus Scale for Extrapyramidal Symptoms score	6.5 ^a	3.4	0.02	0.9	0.07
Akathisia score	1.7	0.1	1.8	0.6	0.5
AIMS total score	2.5	2.9	0.05	0.5	0.8

^ap<0.05.

found in the smokers' group. Higher neuroleptic doses administered to smokers may also reflect clinicians' efforts to control resistant psychotic symptoms, as indicated by smokers' significantly higher scores on the BPRS.

Smokers displayed significantly less neuroleptic-induced parkinsonism, a finding that replicates the study by Decina and colleagues (9). In both studies the effect was highly significant and appeared to be independent of gender, age, and use of anticholinergic agents. The lesser frequency of parkinsonism that we observed was impressive considering that it occurred in patients receiving a twofold higher dose of neuroleptic and that it occurred in the presence of higher levels of akathisia. While Wagner and colleagues (24) found lower levels of parkinsonism only in smokers with durations of illness of less than 7 years, we did not find this to be the case in our study. Only eight (10%) of our patients had been ill less than 7 years, and for the cohort as a whole, duration of illness did not correlate with ratings of parkinsonism. The number of cigarettes smoked daily did significantly correlate with ratings of parkinsonism ($r=0.26$, $df=56$, $p=0.02$).

Whether cigarette smoking directly affects parkinsonism is uncertain. However, just as smoking in the general population appears to protect against onset of idiopathic parkinsonism in later age, smokers in our cohort had begun smoking on average 8 years before starting neuroleptic therapy. This temporal relationship argues in favor of a possible antiparkinsonism effect of smoking, rather than a tendency for patients to smoke in response to extrapyramidal symptoms. It is unlikely that smoking-induced reduction in neuroleptic plasma levels accounts entirely for this effect. Whereas nicotine may reverse some cognitive side effects of anticholinergic agents (42), anticholinergic treatment of smokers and nonsmokers did not differ and so does not account for the antiparkinsonism effect of smoking.

In contrast to the evidence suggesting an antiparkinsonism effect in humans, animal models indicate that nicotine may worsen extrapyramidal symptoms acutely, as nicotine produces catalepsy in mice and enhances neuroleptic-induced catalepsy in rats (17, 43). When administered chronically, nicotine protects against 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine

(MPTP)-induced degeneration of nigrostriatal dopamine neurons in mice, which is an animal model for parkinsonism (44). It has been suggested that nicotine decreases vulnerability of nigrostriatal neurons by desensitizing excitatory nicotinic receptors, thereby reducing firing rates and energy demands of these neurons (45, 46). In addition, nicotine may reduce symptoms of parkinsonism acutely by enhancing release of dopamine in the striatum (47) and, after chronic administration, by lowering brain levels of acetylcholine (48).

The higher level of psychosis in smokers than in nonsmokers, as measured by the positive symptom subscale of the BPRS, was found to be nonsignificant when caffeine intake was controlled for by multiple ANCOVA. Cigarette smoking and caffeine intake correlate in normal subjects as well as in psychiatric patients (49). In our cohort, the number of cigarettes smoked daily correlated with the daily intake of caffeine at the trend level ($r=0.23$, $df=56$, $p=0.05$). Lucas and co-workers (50) recently reported that acute administration of caffeine to schizophrenic patients elevated scores on the BPRS, including positive symptoms such as thought disorder and unusual thought content. However, attempts to demonstrate a psychotogenic effect of caffeine when it is administered over more extended periods have produced inconsistent results (51–53). Mathew and colleagues (54) found significant reductions of cerebral blood flow in schizophrenic patients given a single dose of caffeine but did not observe change in clinical status. Thus, although caffeine use was associated with elevations of psychosis in our cohort, there is little evidence to suggest that caffeine directly contributed to a worsening of clinical status.

Hughes and colleagues (2) noted that cigarette smoking was associated with more severe illness in a heterogeneous sample of psychiatric patients. It has been suggested that schizophrenic patients may smoke in response to symptoms of their illness, as described by 20% of patients interviewed by Glynn and Sussman (6). Normal subjects smoke more heavily when stressed or while experiencing discomfort, possibly reflecting nicotine's reported anxiolytic and antidepressant effects (55). Nicotine also improves concentration and decreases distractibility in normal subjects evaluated with the Stroop Test (34, 56). Patients with schizophrenia

have been shown to be particularly impaired in their performance on this test (57, 58), raising the possibility that schizophrenic smokers may be self-medicating a cognitive deficit. The higher degree of psychiatric impairment in the smokers in our cohort may also reflect levels of impulse control insufficient to stop smoking as well as a lack of motivation, particularly if smoking improves symptoms of their illness or provides one of their few sources of pleasure. Self-medication of more subtle cognitive or affective symptoms during adolescence, before the onset of overt psychotic illness, may also contribute to the higher rate of smoking in schizophrenic patients.

Finally, it has been suggested that persons with histories of affective illness are more likely to smoke because of the antidepressant effect of nicotine and are less likely to stop smoking because abstinence may trigger depressive symptoms (26–28). It is surprising that smokers in our cohort did not score higher than nonsmokers on depression or tension items of the BPRS, despite scoring significantly higher on positive and negative symptoms. It is possible that smoking selectively improves affective symptoms in these patients and that attempts to quit may be thwarted by worsening of these symptoms.

Unlike two prior reports, we did not find more tardive dyskinesia in smokers. The patient samples in which this relationship was found differed from ours in that they consisted of inpatients, were diagnostically heterogeneous, and had lower overall rates of cigarette smoking (11, 25). In addition, the smokers studied by Binder and coworkers (25) were receiving neuroleptic at doses equivalent to doses received by nonsmokers; it is possible that smoking-induced lowering of neuroleptic blood levels in smokers may have resulted in less masking of tardive dyskinesia. While several studies in the general population have demonstrated less parkinsonism in smokers, we are aware of only one study that demonstrated more spontaneous orofacial dyskinesias in smokers (59). Such a finding is complicated by the association of dyskinesia with chronic obstructive pulmonary disease, which may be a consequence of smoking (60).

Our findings must be regarded with some caution. We found that it was generally not possible to blind the rater to the smoking status of patients, so rater bias may have influenced our results. However, the lack of more tardive dyskinesia in smokers and the greater level of positive symptoms were both contrary to our expectations and so were unlikely to represent rater bias. More difficult to assess is whether additional, unmeasured variables may have influenced our findings. Smoking was associated with a number of important factors, such as gender, age, and caffeine consumption. We were able to demonstrate statistically that cigarette smoking remained significantly associated with the level of parkinsonism when each of these factors was controlled. Alcohol and other substance abuse has been associated with smoking in other studies (49) and has been reported at rates as high as 58% in patient populations similar to our cohort (61, 62). The extremely

low rates of substance abuse reported by subjects in our study probably represent underreporting and may have obscured substance abuse as a factor contributing to the association between greater psychopathology and cigarette smoking.

CONCLUSIONS

Three practical conclusions can be drawn from this and other related studies. First, smoking status and caffeine intake are important variables that should be addressed when evaluating data from studies of neuroleptic dose, efficacy, and side effects. Second, work should be continued to identify factors that reinforce smoking behavior in schizophrenic patients so that attempts to reduce their exposure to this serious health risk may be more successful. Finally, if the higher rate of smoking in schizophrenic patients reflects in part self-medication of underlying psychopathology or of medication side effects, we must be cautious in abruptly subjecting schizophrenic smokers to smoke-free therapeutic environments, where symptoms of nicotine abstinence may cloud the clinical picture. Alternative methods for delivering nicotine to these patients may also deserve our attention.

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Sylvian Fissure Size in Schizophrenia Measured With the Magnetic Resonance Imaging Rating Protocol of the Consortium to Establish a Registry for Alzheimer's Disease

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***Objective:** Since previous work indicated smaller than normal temporal lobe structures in schizophrenic patients, the authors tested the hypothesis that this abnormality might be reflected in abnormally large sylvian fissures. **Method:** The subjects were 48 schizophrenic patients and 51 normal comparison subjects matched groupwise with regard to age and sex. CSF spaces (sylvian fissures, temporal lobe sulci, temporal horns, third ventricle, lateral ventricles, and superficial cerebral sulci) were visually assessed with the magnetic resonance imaging rating protocol of the Consortium to Establish a Registry for Alzheimer's Disease (CERAD). **Results:** The sylvian fissures of the schizophrenic patients were found to be bilaterally wider than those of the comparison subjects. There were no other significant differences. **Conclusions:** Schizophrenic patients appear to have larger than normal sylvian fissures, which may reflect smaller superior temporal gyri.*

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When J. Hughlings Jackson proposed in the late nineteenth century that specific brain regions are involved in the pathogenesis of some psychiatric illnesses (1), there was scant evidence to support this hypothesis. Since then, neuropathological studies (2) have shown smaller than normal temporal lobe structures in schizophrenia. Recently, workers in our laboratory (3) showed smaller than normal superior temporal gyri in schizophrenic patients and correlated this to the severity of auditory hallucinations. Since the sylvian fissure overlies the superior temporal gyrus, it would not be surprising if their sizes were inversely proportional. While the finding of large ventricles is well established in schizophrenia (4), few studies have specifically addressed wider than normal sylvian fissures (5, 6).

In the current study we compared the appearance on

magnetic resonance imaging (MRI) scans of cortical and subcortical CSF spaces, including the sylvian fissure, in patients with schizophrenia and in normal comparison subjects according to the MRI rating protocol of the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) (7). This protocol was developed to assess brain atrophy in patients with Alzheimer's disease but, as a standardized method for evaluating the size of CSF spaces, is also applicable to other groups (8).

METHOD

Subjects

The participants in the study were 48 schizophrenic patients and 51 normal comparison subjects. The patients met the criteria for schizophrenia of the Structured Clinical Interview for DSM-III-R (SCID) (9). Each had been hospitalized at least once for this illness but was currently living in the community and receiving outpatient treatment, including neuroleptic medication. No patient had received ECT. The normal comparison subjects were recruited by advertisement and were screened with the SCID. No subject had a history of any of the following: CNS illness, head injury causing unconsciousness for more than 1 hour, headaches of sufficient severity to re-

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TABLE 1. Brain Structure Atrophy in Schizophrenic and Normal Subjects Rated With the MRI Protocol of the Consortium to Establish a Registry for Alzheimer's Disease^a

Structure	Rating of Atrophy ^b				Chi-Square Analysis ^c		
	Schizophrenic Patients (N=48)		Normal Subjects (N=51)				
	Mean	SD	Mean	SD	χ^2	df	p
Sylvian fissures ^d							
Right	0.34	0.31	0.13	0.22	14.04	2	0.0009
Left	0.19	0.24	0.05	0.15	10.64	1	0.001
Temporal lobe sulci							
Right	0.28	0.38	0.10	0.20	9.07	3	n.s.
Left	0.15	0.25	0.11	0.23	0.81	2	n.s.
Anterior temporal horns							
Right	0.12	0.33	0.11	0.21	1.40	2	n.s.
Left	0.07	0.18	0.06	0.16	0.17	1	n.s.
Third ventricle	0.36	0.35	0.24	0.25	8.16	2	n.s.
Lateral ventricles							
Right	0.26	0.40	0.12	0.21	5.72	3	n.s.
Left	0.26	0.41	0.07	0.17	9.37	3	n.s.
Superficial cerebral sulci							
Right	0.41	0.49	0.18	0.36	11.50	4	n.s.
Left	0.37	0.44	0.18	0.37	10.71	4	n.s.

^aSignificant main effects for diagnosis ($F=19.33$, $df=1$, 97 , $p<0.001$) and for side ($F=21.09$, $df=1$, 97 , $p<0.001$); the interaction was not significant ($F=2.23$, $df=1$, 97 , $p=0.13$).

^b0.0=no atrophy, 3.0=most severe atrophy.

^c $2 \times k$ chi-square test, where $k \leq 7$ (k =number of rating categories used in evaluating each of the CSF spaces). Significance defined as $p<0.0045$ with Bonferroni adjustment.

^dHigher mean rating for the right side than for the left side in both the schizophrenic patients (paired $t=-3.68$, $df=47$, $p=0.001$) and the normal subjects (paired $t=-2.68$, $df=50$, n.s.).

quire medical consultation, heavy alcohol or street drug use in the last 12 months, high-dose oral steroid use in the preceding 3 months, or loss of 25% or more of original body weight in the past 12 months.

The subjects were compared groupwise with regard to age and sex; no significant differences were found. The mean age of the schizophrenic patients was 31.5 years ($SD=7.6$, range=18–51), and the mean age of the comparison subjects was 30.3 years ($SD=7.5$, range=18–47) ($t=0.78$, $df=97$, n.s.). Males constituted 67% and 76% of the schizophrenic and comparison groups, respectively ($\chi^2=2.5$, $df=1$, n.s.).

Procedure

We obtained 5-mm-thick, T_2 -weighted (repetition time=2500–3000 msec, time to echo=80–100 msec), axial MRI scans on one of two identical 1.5-tesla GE Signa scanners. The scans were rated by the principal investigator (J.M.S.) under the supervision of a member of the CERAD neuroimaging task force, according to the 1989 draft of the CERAD MRI rating. This method provides photographs of representative MRI scans illustrating atrophic changes of the following CSF spaces: sylvian fissures, temporal lobe sulci, tips of the anterior temporal horns, third ventricle, bodies of the lateral ventricles, and superficial cerebral sulci.

Because many scans fall between these ratings, the developers of the protocol recommended the addition of intermediate ratings. We selected representative scans for intermediate ratings by consensus, thus expanding the number of possible ratings from the origi-

nal four to a total of seven, with 0.0 indicating no atrophy and 3.0 indicating the most severe atrophy. To qualify for a particular rating a structure had to have atrophy that was equal to or greater than that of the representative scan. All structures except the third ventricle were rated separately for each hemisphere.

The rater who assessed the scans was blind to diagnosis. A randomly selected group of 16 scans were re-rated. The values from the first and second ratings were compared, and the kappa coefficient for intrarater reliability was determined to be 0.60 or greater for all measurements.

RESULTS

Table 1 displays the ratings and chi-square values for the structures in the schizophrenic and comparison groups. We performed a $2 \times k$ chi-square analysis in which k was the number of rating categories ($k \leq 7$) used in evaluating each CSF space. Table 2 displays the rating distributions for the right and left sylvian fissures. The schizophrenic patients demonstrated bilaterally wider sylvian fissures, even after Bonferroni adjustment. There were no other significant differences.

In the schizophrenic patients the mean sylvian fissure rating for the right side was significantly higher than the rating for the left, and a nonsignificant difference in the same direction was seen in the comparison subjects (see table 1). A two-way repeated measures analysis of variance, using sylvian fissure rating as the dependent variable, indicated significant main effects for

both diagnosis (schizophrenic versus normal) and side (left versus right). The Diagnosis by Side interaction was not significant.

DISCUSSION

Previous studies have demonstrated wider than normal sylvian fissures in both hemispheres of schizophrenic patients. Pandurangi et al. (5) quantified the maximum width of the sylvian fissures shown by CT in 23 male schizophrenic subjects and 23 male comparison subjects. McCarley et al. (6) visually assessed the CT appearance of CSF spaces, using a 0–4 scale, in nine male schizophrenic patients and nine male comparison subjects, and they also found that the right sylvian fissure was wider than the left in the schizophrenic subjects; unlike us, however, they did not find a similar pattern in the comparison subjects.

Our study has the advantages of the superior spatial resolution of MRI and more subjects, including both men and women. In addition, we used a standardized MRI rating protocol.

Our observation of larger sylvian fissures in schizophrenic patients was subtle, although significant. It is not clear whether this reflects general differences in temporal lobe size between the two groups. Quantitative measures performed in our laboratory (3) indicate a slightly but significantly smaller superior temporal gyral volume in schizophrenic patients than in normal subjects. Unfortunately, relevant volume measurements and indexes of symptom severity were not available for a substantial number of the patients in the current study. Therefore, we did not correlate these with sylvian fissure size.

If a relationship between sylvian fissure size and temporal lobe volume exists, it could reflect either atrophy or hypoplasia. The evidence (10, 11) favors the hypothesis that the structural difference in the brains of schizophrenic subjects is static and due to an early insult or developmental anomaly. However, large sylvian fissures might favor atrophy since CSF space enlargement accompanies shrinkage of surrounding brain mass, whereas a static defect early in development might not change the relationship of the sizes of the fissure and gyrus.

Several studies (12, 13) have suggested lateralized temporal lobe pathology (more on the left) in schizophrenia. Our study does not support these findings. Our failure to replicate the finding of significantly larger than normal ventricles probably reflects the superior sensitivity of previous studies (3, 4), although in our study there was a tendency toward larger ventricles in the schizophrenic patients.

A major limitation of this study was that the subjects had a relatively narrow range of atrophy ratings. This raises doubts about the applicability to schizophrenic patients of a rating scale developed for use with Alzheimer's disease patients, who show a broader range of atrophy.

TABLE 2. Distribution of Ratings of Sylvian Fissure Atrophy in Schizophrenic and Normal Subjects Rated With the MRI Protocol of the Consortium to Establish a Registry for Alzheimer's Disease

Rating of Sylvian Fissure Atrophy ^a	Number of Subjects	
	Schizophrenic (N=48)	Normal (N=51)
Right		
0.0	19	38
0.5	25	13
1.0	4	0
Left		
0.0	30	46
0.5	18	5

^a0.0=no atrophy, 3.0=most severe atrophy.

The CERAD protocol was chosen because our previous experience with it had shown it to be a reliable way of assessing CSF spaces. It is possible that subtler differences could have been revealed by using rating scales with finer gradations developed specifically for schizophrenia. The suggestion to add intermediate ratings is part of the protocol as furnished by CERAD, but representative scans for these were not provided. These were selected specifically for this study by consensus among the authors. We attempted even finer gradations by adding multiple fractional ratings in the range of values we obtained in our patient group but found that we could not reliably rate scans once the gradations became finer than the ones used in this study.

We must conclude that we are approaching the limits of reliability inherent in the use of a visual assessment scale. One developed specifically for schizophrenia would require gradations broad enough that measurements could be made reliably, and it would probably resemble the first few rating categories of the CERAD protocol. At least for this population, the advantages of quantitative volumetric measurements are clear.

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Predicting Feasibility of Day Treatment for Unselected Patients Referred for Inpatient Psychiatric Treatment: Results of a Randomized Trial

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***Objective:** Because previous studies of day treatment as an alternative to inpatient treatment had major disadvantages or methodological shortcomings, the authors conducted a randomized controlled trial to estimate and predict the extent to which day treatment is feasible for unselected patients referred for inpatient treatment. **Method:** Of 160 patients, 57 were randomly assigned to the control condition and 103 were assigned to the experimental condition. Control patients received standard clinical care. In the experimental condition, day treatment was attempted as soon as the patient's condition permitted. The average number of nights per week that experimental patients spent away from the hospital was compared to the average number of nights away for patients under standard care. **Results:** Day treatment was satisfactory for 40% of the experimental patients but was completely infeasible for another 40%. The level of surveillance needed in the first week, physical illness, number of previous admissions, depressive symptoms, and treatment by qualified psychiatrists versus registrars were variables predictive of these differences. **Conclusions:** In this unselected group of patients, no absolute contraindications against day treatment were found. This suggests that the selection criteria applied in nearly all other controlled studies on the subject were unwarranted. The approach used in this study facilitated treatment in the least restrictive environment possible.*

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Every psychiatric treatment modality should face two basic questions: For which categories of patients is it feasible? and How does it affect their psychosocial functioning?

Neither question has yet been answered conclusively for day treatment as an alternative to inpatient treatment. In nine controlled inquiries (1-12) over more than 25 years, day treatment has been studied for a total of 545 patients referred for hospitalization. Nearly one-half participated in the two oldest studies (1-4), which are not well documented. With one exception (1, 2), the patient groups have been selected too stringently to permit unmitigated conclusions. Authors of reviews who have claimed that the second question has been fully (13-15) or partially (16, 17) decided in favor of such day treatment have neglected the limited generalizations that can be drawn from the subjects studied.

Zwerling, Wilder, and Levin (1, 2) conducted the

only controlled study in which the two questions have been addressed conjointly for an unselected group referred for full-time hospitalization, but this study had shortcomings. The randomization ratios fluctuated during enrollment (1), which is undesirable from a methodological point of view (18). Outcome measurement was limited to unstandardized ratings of the patient's psychiatric status and family adjustment by the patient and/or a relative, and these ratings were not assessed at baseline (2). Several essential sociodemographic data were not reported, so evaluation of the equivalence of the control and experimental groups was impossible (1, 2). Nevertheless, this study was important because it did not exclude any patients considered for admission, approaching each patient with the intention to use alternative treatment. This enabled a comparison of patients for whom day treatment turned out to be feasible with those who could not be treated according to that alternative.

Five additional randomized studies on day treatment as an alternative to hospitalization have been published (3-9). Three others applied a weaker design (10-12), comparing patients directly referred to day treatment with globally equivalent groups of inpatients. Such nonrandom allocation can easily produce unbalanced groups (18), as occurred in one study (10): 37% of the

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TABLE 1. Controlled Studies on Day Treatment as an Alternative to Inpatient Treatment

Study	Patients - Considered for Selection	Patients Actually Selected for Study		Assigned to Day Treatment	Assigned to Full Hospitalization	Remarks
		Total				
		N	%			
Random assignment of subjects to groups						
Zwerling and Wilder (1)	378	378	100	189	189	All referred patients included
Kris (3)	—	142	—	71	71	Only relapsed psychotic patients included
Herz et al. (5)	424	90	21	45	45	Study group selected from all referred patients
Washburn et al. (6)	392	59	15	29	30	Study group selected from referred women only
Dick et al. (8)	≥350 ^a	91	≤26	43	48	Study group selected from referred patients with neuroses or personality disorders only
Creed et al. (9)	185	102	55	51	51	Study group selected from all referred patients
No randomization						
Michaux et al. (10)	—	106	—	50	56	75% of subjects were female
Fink et al. (11)	—	86	—	43	43	70% of subjects were female; 67% had not been hospitalized previously
Penk et al. (12)	—	48	—	24	24	Only men included

^aOnly the lower bound of the number of patients considered for selection could be calculated from this study.

patients in the inpatient group, but only 10% in the day treatment group, were from the lowest social class.

All of the studies since 1970 (5–12) were primarily outcome studies of rather stringently selected groups of patients. Stringency, in terms of the percent of potentially eligible patients actually included, is shown in table 1 for each of the randomized studies. Corresponding percentages were not available from the reports on the other three inquiries. Their selection criteria did, however, not differ essentially from those in the randomized studies. Thus, the generalizability of effects identified by these studies appears to be seriously limited; statements as to feasibility of day treatment are necessarily restricted to minorities of patients referred for admission. Only two reports (5, 9) provided (scarce) data on the randomly assigned patients who could not be fully maintained in day treatment.

The typical day treatment patient studied under controlled conditions appears to be not very ill, to not be very violent, to not be homicidal or noncompliant, to have intact family relations, to not live alone, to be able to rely on someone to provide care, to have no physical illness, to be under 65 years of age, to not be certified, and to be female. (An overview of the distributions of sociodemographic and psychopathological variables in the reviewed studies is available from H.K.) The same impression emerges from uncontrolled studies (19–22) attempting to differentiate patients referred for full hospitalization from those referred to day treatment facilities designed to avoid inpatient care.

We conducted a randomized controlled trial in the Netherlands to evaluate the feasibility and effects of day treatment as an alternative to inpatient care. It can be seen as a replication and expansion of the study by Zwerling, Wilder, and Levin (1, 2).

METHOD

Study Design

From November 1986 to March 1988 a total of 160 patients were randomly assigned to two conditions. All patients were referred for inpatient treatment by psychiatric outpatient services or their general practitioners, except four who were self-referred. Data from the case register showed that the referral pattern during the period of enrollment did not differ from that in the 2 years before the study.

Randomization occurred immediately after acceptance of the patient for admission. Assignment was in blocks of 14 patients, with a fixed ratio of nine experimental to five control subjects, resulting in 103 experimental and 57 control patients. Allocation of the majority of the patients to the experimental condition has distinct advantages when it is unclear whether the experimental treatment can be applied to all patients who are eligible (23, 24).

Standardized measures of psychopathology and social functioning were assessed at entry and at 1 and 2 years; the patient's and a relative's satisfaction with treatment and the burden on the family were also assessed. A regional psychiatric case register recorded all contacts of each patient with mental health care providers and institutions during the 2 years of follow-up.

The research team operated independently of the treatment teams.

Patients

Two categories of patients were excluded from the study: forensic patients assessed at court request (because they

TABLE 2. Characteristics of Subjects in Current Study of Day Treatment and Study by Zwerling and Wilder (1)

Characteristic	Patients Assigned to Full-Time Hospitalization (N=57) ^a		Patients for Whom Day Treatment Was Attempted (N=103) ^a		Prevalence (%) in Zwerling and Wilder's Patients for Whom Day Treatment Was Attempted (N=189) ^{a,b}
	N	%	N	%	
Female	23	40.4	57	55.3	56.7
Age (years)					
18-24	8	14.0	13	12.6	—
25-44	27	47.4	53	51.5	—
45-64	12	21.1	26	25.2	—
≥65	10	17.5	11	10.7	—
Living alone	22	38.6	29	28.2	—
Marital status					
Single	22	38.6	40	38.8	—
Married	19	33.3	41	39.8	—
Divorced	12	21.1	14	13.6	—
Widowed	4	7.0	8	7.8	—
Education					
College/university	4	7.4	15	15.6	—
Secondary	10	18.5	17	17.7	—
Elementary	38	70.4	58	60.4	—
None	2	3.7	6	6.3	—
Unemployed	48	87.3	86	88.7	—
Disability pension	30	54.5	54	55.7	—
Involuntary admission	6	10.5	8	7.8	—
Previous admissions					
None	24	43.6	38	36.9	48.2
1	8	14.5	21	20.4	24.1
2	5	9.1	19	18.4	13.2
≥3	18	32.7	25	24.3	14.4
Psychiatric diagnosis					
Current study ^c					
Substance addiction/abuse	11	19.3	13	12.6	
Schizophrenia	17	29.8	36	35.0	
Affective psychosis	7	12.3	10	9.7	
Depression or anxiety	9	15.8	24	23.3	
Other <i>DSM-III</i> diagnoses	13	22.8	20	19.4	
Zwerling and Wilder study ^d					
Schizophrenia					39.7
Affective psychosis					10.0
Brain syndromes					20.6
Involutional psychosis					4.2
Other psychosis					2.1
Neurosis or personality disorder					23.3

^aPercents based on varying numbers because not all data were available for all subjects.^bData on the control group of Zwerling and Wilder were not published.^c*DSM-III* diagnoses used.^dClassification system not specified.

were not admitted for treatment) and patients suffering from any form of dementia. The latter were referred to special institutions. Their exclusion was made explicit, since they might be admitted because of an initially false diagnosis. All other admitted patients from a designated catchment area were included, irrespective of age, certification, or any other variable. Zwerling and Wilder's patient group (1) probably matches our cohort best; the scarcity of published data from their study prohibits a definite conclusion. The semiurban catchment area of 95,000 inhabitants is located in the northeastern part of the Netherlands. It is less prosperous than other areas and has a relatively high rate of unemployment.

Essential psychopathological and sociodemographic data are presented in table 2. The total group did not differ from all patients admitted to psychiatric hospitals

in the Netherlands in 1984. The experimental and control groups were statistically equivalent on *DSM-III* diagnoses and sociodemographic characteristics. The last column shows corresponding data adapted from the Zwerling and Wilder study for their experimental patients only. Information on their control subjects was not published. Our study includes more patients with three or more previous admissions and fewer admitted for the first time. The *DSM-III* diagnoses we report are, of course, only roughly comparable to the diagnoses in the Zwerling and Wilder study.

Conditions

The trial was conducted in a modern 500-bed psychiatric hospital. In the control condition, the patients

TABLE 3. Number of Nights Spent Away From the Hospital by Patients Who Received Full-Time Hospitalization and Patients for Whom Day Treatment Was Attempted^a

Mean Number of Nights Away From Hospital per Week	Patients Assigned to Full-Time Hospitalization (N=55)		Patients for Whom Day Treatment Was Attempted (N=97)	
	N	%	N	%
0	20	36.4	19	19.6
>0 to 1	11	20.0	9	9.3
>1 to 2	15	27.3	11	11.3
>2 to 3	6	10.9	10	10.3
>3 to 4	3	5.5	10	10.3
>4 to 5	0	0.0	6	6.2
>5 to 6	0	0.0	13	13.4
>6 to 7	0	0.0	19	19.6

^a $z=5.04$, $p=0.0000$ (Mann-Whitney test for independent samples). The mean for the patients who received full-time hospitalization was 1.02 nights ($SD=1.02$), and for the experimental patients it was 3.17 nights ($SD=3.54$).

were treated according to standard hospital care, which included 24-hour hospitalization, medication, regular contacts with a psychiatrist, occupational therapy, and in selected cases, individual, group, behavioral, creative, or psychomotor therapy.

In the experimental condition, day treatment was initiated 1) at once, 2) after some time had elapsed, or 3) not at all, depending on the patient's condition and social situation. The patient's condition and social situation were assessed by a team headed by a psychiatrist or registrar. Close relatives or the patient's partner were asked to be present. The procedure also served to provide the patient and the relatives with extensive information about the support available. On that occasion it was decided by the available parties whether to initiate day treatment at once or to postpone that decision to a later date. All decisions then and later were the final responsibility of the attending psychiatrist or registrar. (In the Netherlands a registrar is a physician seeking registration as a specialist; in psychiatry a 4-year training is required.) The general clinical criterion for keeping a patient in the hospital overnight was danger to self or to others.

The day treatment lasted from 8:30 a.m. to 4:30 p.m. (weekends excluded). It was provided either in a new day center on the hospital grounds, with a specialized multidisciplinary program, or in a regular clinical unit. During day treatment, nights in the hospital could be prescribed; such a prescription was based on the same criteria and authority as previously stated. While the patient was at home, staff could be contacted by telephone on a 24-hour basis. The hospital staff collaborated with the regional psychiatric service outside the hospital, which could at all times render assistance at home and was involved in aftercare (25).

Measures

Feasibility was defined as the average number of nights per week patients spent away from the hospital

according to plan. The average number of nights was calculated by dividing the sum of the nights away from the hospital by the duration in weeks of the treatment episode. This procedure served to render patients with treatment episodes of different durations comparable. This yields a maximum score of 7 for patients fully in day treatment and a minimum score of 0 for patients fully hospitalized. For the control group, this variable denotes the average number of night leaves given in standard care.

This information was missing for eight patients; no differences were found between them and the other patients.

Zwerling and Wilder (1, p. 171) constructed an ordinal variable not fully comparable to ours. Their category II, which included patients (22%) who were transferred to wards more than once or were transferred once for more than 2 nights, covers a wide range; for instance, 12 of their patients were boarded longer than 14 nights, but how much longer was not reported.

For reasons explained further on, the predictor variable "level of patient's protection" was determined. It was measured on a 6-point scale: 6=no need of surveillance; 5=surveillance at fixed times at the group level; 4=permanent surveillance at the group level, occasional interruptions possible; 3=permanent surveillance at the group level; 2=permanent surveillance at the individual level most of the time and on the group level some of the time; and 1=permanent surveillance at the individual level all of the time. Scores for the morning, afternoon, evening, and night of each day of treatment were provided by the attending nurses. The observation sheets used were tested extensively in a pilot study on 40 patients.

Data Analysis

Distributions of the feasibility variable in the control and experimental conditions were determined. The hypothesis that the experimental patients would rank higher on this variable was evaluated with the Mann-Whitney test for rank orders (one-tailed, $p<0.01$).

Predictors of differences in feasibility among the experimental patients were explored with analysis of variance (ANOVA), simple correlation, multiple regression, and discriminant analysis.

RESULTS

Table 3 shows that the average number of nights the patients in the experimental condition spent away from the hospital substantially exceeded the average for the control subjects. More than one-third of the control subjects did not leave the hospital at all during their episodes of treatment; 59.8% of the experimental subjects spent more than 2 nights a week away from the hospital, compared with 16.4% of the control subjects. If it is considered desirable for patients to be treated in the least restrictive environment possible, this constitutes an important dif-

TABLE 4. Selected Predictors of Number of Nights Spent Away From the Hospital by 97 Patients for Whom Day Treatment Was Attempted

Predictor Variable	N	Nights Away From Hospital per Week		One-Way ANOVA			Explained Variance (%) ^a
		Mean	SD	F	df	p	
Sex				2.28	1, 95	0.56	0
Female	54	3.04	2.54				
Male	43	3.35	2.55				
Living situation				0.001	1, 95	0.97	0
Living alone	28	3.17	2.74				
Not living alone	69	3.17	2.47				
Marital status				1.45	3, 93	0.24	4
Single	37	3.05	2.70				
Married	40	3.67	2.28				
Divorced	13	2.02	2.52				
Widowed	7	3.18	2.88				
Age (years)				0.75	3, 93	0.52	0
18-24	11	3.25	2.64				
25-44	50	3.44	2.70				
45-64	26	2.55	2.41				
≥65	10	3.41	1.91				
Type of admission				0.68	1, 95	0.41	0
Involuntary	8	2.47	2.49				
Voluntary	89	3.24	2.55				
Previous admissions				1.60	3, 93	0.19	4
None	35	3.70	2.70				
1	19	2.36	2.06				
2	19	3.60	2.88				
≥3	20	2.73	2.24				
DSM-III diagnosis				0.70	4, 92	0.60	3
Substance addiction/abuse	13	3.58	2.74				
Schizophrenia	33	2.65	2.59				
Affective psychosis	10	3.24	2.29				
Depression or anxiety	22	3.73	2.48				
Other	19	3.13	2.58				
Reasons for admission							
Threat to self				0.38	1, 95	0.54	0
Yes	19	3.50	2.56				
No	78	3.10	2.54				
Threat to others				0.30	1, 95	0.59	0
Yes	6	3.72	3.04				
No	91	3.19	2.52				
Depressive symptoms				9.02	1, 95	0.003	9
Yes	19	4.68	2.15				
No	78	2.81	2.50				
Clinician				11.53	1, 95	0.001	11
Qualified psychiatrist	52	3.95	2.54				
Registrar	45	2.28	2.25				

^aMeasure for explained variance was η^2 .

ference. We consider the 40.2% of the experimental patients who left the hospital no more than 2 nights a week on average as unsuitable for day treatment. A satisfactory degree of day treatment, i.e., more than 4 nights at home per week on average, was attained by 39.2% of the experimental patients. As stated before, the results from the Zwerling and Wilder study (1) are not quite comparable to ours as their outcome variable was less specific. Their results were as follows: 34% of their experimental patients were treated entirely on wards, 22% needed more than one transfer to wards or one transfer lasting longer than 2 nights, an additional 5% were transferred once to hospital wards for 1 or 2 nights, and 39% were fully in day treatment.

Test results for the potential predictors of the feasibility of day treatment, assessed with one-way ANOVA, are

shown in table 4. Several variables thought to contraindicate day treatment did not appear to be prohibitive after all. Most prominent of these—and common criteria for exclusion—are substance addiction/abuse, compulsory admission, living alone, and old age. All of the subgroups in table 4 had considerably higher mean feasibility values, i.e., spent considerably more time away from the hospital, than the control group. Patients treated by qualified psychiatrists were substantially more successful than patients treated by registrars.

The best single predictor of feasibility was the most liberal level of protection under which the patient could be managed at least once in the first week of treatment ($r=0.54$, $df=89$, $p<0.001$). Average level of protection in the same week was also a good predictor ($r=0.46$, $df=89$, $p<0.001$). The most liberal level, departing from

TABLE 5. Multiple Regression Analysis of Nights Spent Away From the Hospital by Patients for Whom Day Treatment Was Attempted^a

Predictor	Cumulative R ²	Significance of Change	Zero-Order Correlation With Nights Away From Hospital (df=89)	
			r	p
Level of surveillance in first week	0.29	<0.001	0.54	<0.001
Physical illness	0.32	<0.05	-0.29	<0.01
Lack of previous admissions	0.36	<0.05	0.19	<0.05
Depressive symptoms as reason for admission	0.39	<0.05	0.28	<0.01

^aF=13.60, df=4, 86, p=0.0000; R²=0.36 after correction for shrinkage.

the average level of protection, implies that the patient's condition has at least once been such that protection could be alleviated. Such quick initial improvement in the first treatment week seems to heighten the patient's chances with day treatment slightly, as is reflected by the greater predictive power of the most liberal level of protection over the average level.

Multiple regression analysis (table 5) identified four predictors that together explained 39% of the variance—36% if corrected for shrinkage (26). The most liberal level of protection possible in the first treatment week emerged again as the most powerful predictor. Physical illness at entry had a negative association with feasibility. If depressive symptoms—irrespective of *DSM-III* diagnosis—were the immediate and main cause of admission, then the patient's likelihood of success in day treatment was increased. Patients accepted for first admission had somewhat better chances too. Variables derived from baseline measurement of psychopathology and social functioning did not increase the multiple correlation.

Two feasibility groups were contrasted by discriminant analysis: a "failure" group, which contained patients who each averaged 4 or fewer nights per week away from the hospital, and a "success" group, who averaged more than 4 nights per week. The analysis yielded a highly significant discriminant function (Wilks's $\lambda=0.77$, $\chi^2=22.01$, df=4, p<0.0002). The discriminant function was dominated by the four variables identified by multiple regression analysis plus the variable indicating whether the patient's doctor was a qualified psychiatrist or a registrar. From the discriminant function, actual group membership could be predicted correctly in 74% of the cases.

DISCUSSION

If success in the Zwerling and Wilder study (1) is narrowed down to their two highest categories of patient

outcome and if our criterion for success is assumed to be equal to theirs, their percentage of successfully treated patients (44%) is similar to ours (39.2%). Creed et al. (9) claimed that 68.7% of their patients were successfully treated with day treatment. If their data are corrected for the rejection of 45% of their patients for day treatment before randomization (see table 1), their success rate is 37.8%. The convergence of these three studies, two without selection criteria and one (9) with more liberal criteria than in the remaining studies, is remarkable. One is tempted to speculate that this 40% success rate constitutes an upper limit. However, more evidence from new studies is needed. Contributions to the comparability of such studies would be more detailed specification of the circumstances under which they are conducted and the application of the same outcome measures, e.g., feasibility as defined in this paper. Preferably, new studies should be coordinated in order to vary circumstances and other variables systematically.

One circumstance specific to our study needs closer attention: roughly one-half of the patients were treated by registrars. These patients spent considerably fewer nights away from the hospital than patients treated by qualified psychiatrists. This fact might reflect the limited professional experience of registrars, inducing feelings of insecurity concerning the risks involved and thus resulting in conservative decisions. The authors of one British report (27) attributed the failure to even start a randomized day treatment experiment mainly to the conservatism of trainee psychiatrists. Our success rate might have been considerably higher if the patients had been treated by qualified psychiatrists only.

The degree of predictability we established, 36% explained variance and 74% correct classifications, is substantial in clinical research. To our knowledge, predictability studies comparable to ours have not been conducted in day treatment settings. Emergency room studies (28) of the decision to hospitalize or not seem most related. The extent to which they succeeded in predicting the decisions reached might corroborate the strength of our findings. In one study (29), 18% explained variance was reported. Another (30) explored differences between clinicians and many other predictors. In the final analysis it succeeded in classifying 96% of the nonhospitalized patients correctly. Only 60% of the patients eventually hospitalized were correctly classified by means of the variables in hand.

We assume that the supportive facilities offered during day treatment episodes contributed highly to the maintenance in day treatment of categories of patients who seem less suited for it, e.g., patients who lived alone and patients who were involuntarily admitted. Practical or psychological support by telephone was available around the clock. If circumstances demanded, day treatment was interrupted by hospitalization for one or a few nights or the regional psychiatric service rendered assistance at home. Agreement to follow day treatment implied the formal guarantee to the patient that he or she could call on these facilities at any time.

If the patient lived with relatives or a partner, the same guarantee applied to them. Such a guarantee had practical meaning, of course, but it also created a psychological climate indicating that an appeal for help would never be turned down.

There is at least one group of patients that has never been explicitly excluded from controlled studies of day treatment: patients admitted for depressive symptoms (this is also true of most uncontrolled studies, e.g., the study by Craft [31], one of the oldest). To the best of our knowledge, no reports have ever indicated that as a group they fail in day treatment. Our study is no exception; of all subgroups, depressed patients had the highest success rate.

Probably our most important finding is that there appear to be no absolute contraindications against day treatment. This finding contradicts the exclusion criteria prevailing in controlled studies. If we accept the premise that each patient is entitled to the least restrictive environment possible, given his or her condition (32), it seems to be well worth considering day treatment as a potential alternative to hospitalization for all patients.

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Tardive Dyskinesia in Elderly Psychiatric Patients: A 5-Year Study

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Objective: The authors investigated the prevalence of tardive dyskinesia among elderly psychiatric patients who had never received neuroleptic medication before their first hospitalization. **Method:** The study was performed in the geriatric psychiatry unit of a university-affiliated hospital in Canada and involved all first-admission patients admitted from September 1984 through August 1989 who had never taken neuroleptic drugs. In September and October 1989, the patients who were available for follow-up were examined and given ratings on the Abnormal Involuntary Movement Scale to establish the presence or absence of tardive dyskinesia. The patients' records were reviewed for information on age, diagnosis, duration of hospitalization, neuroleptic treatment received after admission, anticholinergic drugs received, and drug-free periods. **Results:** Of the 162 patients who were available and whose data were analyzed, a total of 99 had been treated with neuroleptics, and 35 (35.4%) of these were found to have tardive dyskinesia. Two of the 35 also had tardive dystonia. Significantly more patients with major depression than patients with primary degenerative dementia or delusional psychosis had tardive dyskinesia. **Conclusions:** This study confirms the higher vulnerability of elderly psychiatric patients treated with neuroleptics to the development of tardive dyskinesia. The authors stress that caution is especially necessary when neuroleptics are prescribed for older patients with major affective disorders.
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Tardive dyskinesia, a neuroleptic-induced movement disorder, has been reported to be more prevalent in patients whose medication is started late in their illness (1) and in newly treated elderly psychiatric patients (2-4). Thus, psychiatric patients in the geriatric age group are at risk, and there are some estimates that tardive dyskinesia may develop in a short period in almost half of neuroleptic-treated patients in this age population (4, 5). Although tardive dyskinesia may occur in a large number of elderly psychiatric patients, spontaneous dyskinesia may also occur in an average of 5% of these patients without prior neuroleptic therapy (6). Thus, when these patients are studied, it is important to provide a comparison group of patients who have never received neuroleptics in order to account for the possible appearance of spontaneous dyskinesia.

In our hospital, we have been studying the prevalence of tardive dyskinesia in newly treated elderly psychiat-

ric patients for the past 5 years. In 1988 we reported (4) on a 2-year study that started in September 1984 and ended in August 1986 which involved 78 first-admission patients, 39 of whom received neuroleptics and 39 who never received neuroleptics. Of the patients who received neuroleptics, 16 (41.0%) developed tardive dyskinesia after a mean of 14.8 months (SD=8.3) of continuous neuroleptic therapy. This is a slightly lower proportion than that in a more recent study by Saltz et al. (5), who found that 48.9% of their subjects developed tardive dyskinesia after 48 weeks of cumulative neuroleptic exposure.

The present study extended our previous one (4). We report on the prevalence of tardive dyskinesia in patients who were treated with neuroleptics for up to 60 months (5 years) during the period from Sept. 1, 1984, to Aug. 30, 1989.

METHOD

Patients admitted for the first time to the geriatric psychiatry unit at our hospital (minimum age=65 years; catchment area=300,000 population) who had never received neuroleptics before admission—as confirmed

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by detailed medication histories obtained from the patients, relatives, and referring physicians—were evaluated for the presence of movement disorders with the Abnormal Involuntary Movement Scale (AIMS) (7). All patients who had received neuroleptics before admission were excluded from the study.

The AIMS measures the severity of tardive dyskinesia on a scale of 0 (no tardive dyskinesia) to 4 (severe tardive dyskinesia) in each of seven body areas. Because the AIMS does not measure dystonia, we also added the dystonia items of the Simpson Rating Scale (8) to the AIMS, as previously described in our tardive dystonia studies (9, 10). We followed the criteria set by Jeste and Wyatt (11) for determining the presence of tardive dyskinesia, i.e., a minimum AIMS score of 2 (mild) for one body area. We used this same criterion as the minimum in our previous studies (1, 12).

Patients admitted for the first time to our unit were also evaluated for spontaneous dyskinesia before they received any neuroleptic treatment and again during the study period, i.e., during September–October 1989.

A total of 251 patients (95 men and 156 women) who had never received neuroleptics were admitted to the hospital for the first time during the period from September 1984 through August 1989. For reexamination for the presence of tardive dyskinesia or spontaneous dyskinesia, patients were visited in their homes, nursing homes, foster homes, outpatient clinics, or inpatient unit. The examiner was blind to their neuroleptic intake since admission to the hospital. Diagnoses were made according to *DSM-III* criteria and were confirmed by two independent investigators using the Hamilton Rating Scale for Depression (13), the Mini-Mental State examination (14) for primary degenerative dementia, and the Brief Psychiatric Rating Scale (15) for delusional disorders.

Following the examination of each patient, the files were reviewed to record whether the patient had received neuroleptics or not, to identify diagnosis, and to study in detail the patient's neuroleptic intake until the end of August 1989. Drug-free periods of 1 month or more were also recorded. (The chart reviews were conducted without knowledge of the patients' current tardive dyskinesia status.) Total neuroleptic time was defined as the total time that a patient received neuroleptic treatment minus the drug-free periods. Neuroleptic dosage was translated into chlorpromazine equivalents with Davis's formulas (16), except for pimozide dose, which was translated into chlorpromazine equivalents (0.5 mg equivalent to 100 mg of chlorpromazine) according to Baldessarini's method (17), and fluphenazine injection (25 mg i.m. every 2 weeks equivalent to 300 mg/day of chlorpromazine), which was calculated according to the formula of Nestoros et al. (18, 19).

RESULTS

During the 5-year period between September 1984 and August 1989, of the 251 first-admission patients

who had not received neuroleptics, 64 (31 men and 33 women) died; their mean age was 79.3 years (range=66–95). Of these, 43 were diagnosed as having primary degenerative dementia, nine bipolar disorder, eight delusional disorder, and four alcoholic dementia. In addition, 25 patients (10 men and 15 women) could not be contacted for the follow-up. Their mean age was 71.5 years (range=70–85). Of these, 18 had diagnoses of major depression, six delusional disorder, and one primary degenerative dementia.

For the final analysis, 162 patients (54 men and 108 women) were available for reexamination during the months of September and October 1989. Of these, 99 (29 men and 70 women) had been prescribed neuroleptics at some point during the 5-year period covered by the study, while 63 (25 men and 38 women) had never received neuroleptics. (Anticholinergic drugs are not prescribed on a prophylactic basis in the geriatric psychiatry unit but were prescribed for some patients as needed.) The mean age of the patients who did not receive neuroleptics was 76.4 years (range=66–95). Of these, 22 had diagnoses of primary degenerative dementia, 38 major depression, one delusional disorder, and two alcoholic dementia.

Prevalence of Spontaneous Dyskinesia

Of the 251 patients admitted for the first time to our unit, 10 (six men and four women) showed evidence of spontaneous dyskinesia before any neuroleptic treatment was instituted. This constitutes 4.0% of the total patient population (6.3% of the men and 2.6% of the women). Their mean age was 77.7 years (range=70–86). Of the 10 patients with spontaneous dyskinesia, five were diagnosed as suffering from primary degenerative dementia, four from major affective disorders, and one from delusional psychosis. All of them exhibited mild bucco-oral movements. No other body areas were affected.

At follow-up, five of the patients with spontaneous dyskinesia had died. Of the other five patients, one had received neuroleptics, and her abnormal movements had disappeared. She also showed no evidence of tardive dyskinesia. Four of the patients who received no neuroleptics continued to exhibit mild bucco-oral movements. Thus, four (6.3%) of 63 patients who received no neuroleptics showed evidence of spontaneous dyskinesia at follow-up.

Prevalence of Tardive Dyskinesia

The characteristics of the patients who received neuroleptics (N=99) are presented in table 1. The patients without tardive dyskinesia were significantly older than the patients with tardive dyskinesia. The prevalence of tardive dyskinesia in the patient population was 35.4% (35 of 99). More men (13 of 29, or 44.8%) than women (22 of 70, or 31.4%) had tardive dyskinesia, but this difference was not statistically significant ($\chi^2=1.6$, $df=1$). However, if we apply the criteria of Schooler and

TABLE 1. Characteristics of 99 Neuroleptic-Treated Patients With or Without Tardive Dyskinesia

Variable	Patients With Tardive Dyskinesia						Patients Without Tardive Dyskinesia						Analysis	
	Men (N=13)		Women (N=22)		Total (N=35)		Men (N=16)		Women (N=48)		Total (N=64)		t	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	(df=97)	p
Age (years)	73.5	5.4	74.9	5.1	74.5	5.0	77.1	6.3	77.6	7.1	77.4	6.9	2.30	<0.02
Duration of hospitalization (months)	37.9	18.6	21.2	20.0	26.4	21.1	10.1	10.9	13.8	16.8	12.9	15.5	3.46	<0.001
Duration of neuroleptic treatment (months)	31.8	16.9	24.6	18.0	27.3	17.7	16.6	16.2	17.3	17.0	17.1	16.6	2.80	<0.005
Drug-free period (months)	1.8	3.3	6.0	11.3	4.4	9.3	3.4	8.2	1.2	2.8	1.8	4.8	1.86	<0.07
Total amount of neuroleptic (g)	209.9	224.6	69.5	97.8	129.5 ^a	169.6	81.8	116.2	54.2	73.3	61.1 ^b	85.9	2.67	<0.009
Total amount of antiparkinsonian drug (mg)	571.9	1362.4	1005.9	2207.4	842.1	1925.9	154.3	484.1	264.1	808.0	239.7	740.8	2.20	<0.03
Present neuroleptic dose (mg/day in chlorpromazine equivalents)	106.2	113.2	64.8	89.9	76.4 ^c	91.5	173.7	243.0	80.7	159.4	120.7 ^d	194.7	1.28	<0.20
AIMS ^e score	5.2	2.5	4.9	2.8	5.0	2.6	—	—	—	—	—	—	—	—

^aRange=8–777 g.^bRange=3–467 g.^cRange=0–375 mg/day.^dRange=0–800 mg/day.^eAbnormal Involuntary Movement Scale.

Kane (20) for minimum manifestation of tardive dyskinesia (i.e., two areas of the body with a minimum AIMS rating of 2 or one area with a rating of 3), then the prevalence of tardive dyskinesia was 30.3% (30 of 99), and significantly more men (13 of 29, or 44.8%) than women (17 of 70, or 24.3%) exhibited tardive dyskinesia ($\chi^2=4.07$, $df=1$, $p<0.05$).

Eleven of the patients had mild tardive dyskinesia, 21 had moderate tardive dyskinesia, and three had severe tardive dyskinesia (table 2). The bucco-oral area was affected in all 35 of these patients. In addition, six women were affected in their arms or legs. Tardive dystonia (torticollis) was present in two men; their family members did not show evidence of movement disorders. These two patients also had mild bucco-oral tardive dyskinesia. Thus, the prevalence of tardive dystonia in our patients was 2.0%, and 6.9% in the men.

Neuroleptic Intake

Patients who received neuroleptics were treated for a mean of 20.7 months (range=1–60 months). This indicates the duration of actual neuroleptic treatment, excluding drug-free periods. Patients who developed tardive dyskinesia received significantly longer neuroleptic treatment than patients without tardive dyskinesia (table 1).

Of the 99 patients who received neuroleptics, 58 received one neuroleptic: 47 received haloperidol, four received pimozide, three perphenazine, two chlorpromazine, and one each thioridazine and fluphenazine. Of the haloperidol-treated patients, 14 (29.8%) developed tardive dyskinesia. Of the pimozide-treated patients, two developed tardive dyskinesia. No tardive dyskinesia developed when the other medications were given

alone. Of the remaining neuroleptic-treated patients, 31 received two neuroleptics, nine received three neuroleptics, and one received four neuroleptics.

As shown in table 1, patients with tardive dyskinesia also received significantly more total neuroleptic medication than patients without tardive dyskinesia. Men with and without tardive dyskinesia received a greater total amount of neuroleptics than women in the same groups.

Also noted in table 1, the present dose of neuroleptic drug was not significantly different for the patients with and without tardive dyskinesia. Equal proportions of patients with tardive dyskinesia (13 of 35, or 37.1%) and without tardive dyskinesia (24 of 64, or 37.5%) were not receiving neuroleptics at the time of the examination.

Duration of Neuroleptic Therapy

Of the 48 patients who received 1–12 months of continuous neuroleptic treatment, 11 (22.9%) developed tardive dyskinesia, compared to seven (50.0%) of the 14 who received neuroleptics for 13–24 months. Of the 12 patients who received neuroleptics for 25–36 months, four (33.3%) developed tardive dyskinesia, compared to eight (57.1%) of the 14 who received neuroleptics for 37–48 months. Of the 11 patients who received neuroleptics for 49–60 months, five (45.5%) developed tardive dyskinesia.

Eighteen (51.4%) of the 35 patients with tardive dyskinesia developed the side effect within the first 24 months of continuous neuroleptic therapy.

Of the 35 patients with tardive dyskinesia, 12 (34.3%) had drug-free periods, compared to 20 (31.3%) of the

64 patients without tardive dyskinesia. The mean numbers of drug-free months for the two groups were not significantly different (table 1).

Other Factors

Age. As shown in table 2, there was no indication that aging increases the chances of developing tardive dyskinesia. In fact, if we divide the patient population into 10-year age groups, we find that of the 53 patients in the age range of 65–75 years, 23 (43.4%) showed evidence of tardive dyskinesia, compared to 10 (26.3%) of the 38 in the next age group (76–85 years) ($\chi^2=2.79$, $df=1$, n.s.).

Antiparkinsonian medication. Patients with tardive dyskinesia received significantly more antiparkinsonian drugs than patients without tardive dyskinesia, as shown in table 1. Of the 35 patients with tardive dyskinesia, 19 (54.3%) received antiparkinsonian drugs, compared to 20 (31.3%) of the 64 patients without tardive dyskinesia ($\chi^2=4.11$, $df=1$, $p<0.05$, with Yates' correction). Two of the men with tardive dyskinesia, two of the men without tardive dyskinesia, and one woman without tardive dyskinesia received amantadine as their antiparkinsonian agent.

Diagnosis. Of the 99 patients receiving neuroleptics, 49 were diagnosed as suffering from primary degenerative dementia. Of these, 12 (24.5%) were found to have tardive dyskinesia, compared to 12 (60.0%) of 20 with the diagnosis of major depression, a statistically significant difference ($\chi^2=6.41$, $df=1$, $p<0.03$, with Yates' correction). This difference is still significant if Schooler and Kane's criteria are applied (11, or 22.4%, of the 49 patients with dementia and 10, or 50.0%, of the 20 with major depression; $\chi^2=3.87$, $df=1$, $p<0.05$, with Yates' correction). This difference was not due to a longer duration of neuroleptic treatment (for dementia patients, mean=26.3 months, SD=17.4, range=2–53 months; for depressed patients, mean=22.1 months, SD=15.0, range=8–60 months) or to the total amount of neuroleptic treatment in either diagnostic category (for dementia patients, mean=94.8 g, SD=44.1; for depressed patients, mean=67.6 g, SD=27.7).

Of the 23 patients with delusional (paranoid) disorder, six (26.1%) developed tardive dyskinesia. The difference between the proportion of patients with delusional (paranoid) disorder and the proportion with major depression (60.0%) who developed tardive dyskinesia was statistically significant ($\chi^2=4.97$, $df=1$, $p<0.05$). Of the seven patients with alcoholic dementia, five (71.4%) developed tardive dyskinesia.

Other medications. Of the 35 patients with tardive dyskinesia, 12 (34.3%) received no concomitant medications, compared to 42 (65.6%) of the 64 patients without tardive dyskinesia. Antidepressants were prescribed for 16 (45.7%) of the patients with tardive dyskinesia, compared to nine (14.1%) of the patients without tardive dyskinesia. Antihypertensives (mainly diuretics and methyl dopa) were prescribed for five patients with tardive dyskinesia (14.3%) and three pa-

TABLE 2. Distribution of 99 Neuroleptic-Treated Patients by Age Group

Item	Age (years)				
	65–70	71–75	76–80	81–85	86 or Older
Patients with tardive dyskinesia					
Mild					
Men	0	0	2	0	0
Women	3	3	2	0	1
Moderate					
Men	4	3	1	1	0
Women	2	6	3	1	0
Severe					
Men	2	0	0	0	0
Women	0	0	1	0	0
Patients with tardive dyskinesia as a percentage of all patients in age group					
Men	60.0	37.5	60.0	20.0	0.0
Women	33.3	45.0	35.3	9.1	14.3
Patients without tardive dyskinesia					
Men	4	5	2	4	1
Women	10	11	11	10	6
All patients					
Men	10	8	5	5	1
Women	15	20	17	11	7

tients without tardive dyskinesia (4.7%). Antidiabetics were prescribed for three patients with tardive dyskinesia (8.6%), compared to two patients without tardive dyskinesia (3.1%). Digoxin was prescribed for three patients with tardive dyskinesia (8.6%) and four patients without tardive dyskinesia (6.3%). Levothyroxine sodium was prescribed for two patients with tardive dyskinesia (5.7%) and one patient without tardive dyskinesia (1.6%). Lorazepam was prescribed for 10 patients with tardive dyskinesia (28.6%) and 19 patients without tardive dyskinesia (29.7%).

DISCUSSION

The prevalence of tardive dyskinesia in an elderly population recruited over 5 years, treated continuously with neuroleptics for a mean of 20.7 months (range=1–60 months), was 35.4%. On the other hand, of 63 patients who received no neuroleptics, four (6.3%) showed spontaneous dyskinesia. These findings are compatible with those in the published studies of comparable patient populations (2, 3, 5).

Although for many years one of the few consistent research findings has been that the prevalence of tardive dyskinesia increases with age, relatively few studies have been devoted to those patients who receive neuroleptics for the first time after age 65. Crane and Smeets (2) found that tardive dyskinesia developed in 39% of 39 patients (median age=74 years, range=63–89) who were followed for a period up to 28 months. Lieberman et al. (3) found that tardive dyskinesia developed in

16.5% of 79 elderly patients who were treated with neuroleptics for 18 months (mean age=85.5 years, range=65–99). Finally, Saltz et al. (5) found that tardive dyskinesia developed in 49% of 84 patients treated with neuroleptics for a mean of 16.7 weeks (mean age=76.6 years, range=57–96). The mean prevalence of tardive dyskinesia in these studies is 34.2%, which is close to the 35.4% in our present study.

Women have been overrepresented in all the studies dealing with elderly psychiatric patients, but we found the prevalence of tardive dyskinesia to be nonsignificantly higher in the men than in the women, if the more liberal Jeste and Wyatt criteria (11) are applied. And, if the Schooler and Kane criteria (20) are applied, tardive dyskinesia appears to have been significantly more prevalent in the men than in the women. Tardive dyskinesia was found to be equally distributed in both sexes in a recent study of a similar patient population (5).

Our study is the first to indicate the prevalence of tardive dystonia in an elderly psychiatric population. We found that tardive dystonia was present in 2% of the treated patients. This corresponds to findings in our previous studies (9, 10), where tardive dystonia occurred in 2% of a younger population.

Spontaneous dyskinesia was found in 4% of our patient population, corresponding to the weighted mean of 4% in the most recent reviews on the subject (6, 11, 21, 22). At the end of the 5-year period we studied, four (6.3%) of 63 patients who never received neuroleptics exhibited spontaneous dyskinesia. None of the 63 patients had developed *de novo* spontaneous dyskinesia or tardive dyskinesia when reexamined.

In our study, we found that patients with tardive dyskinesia stayed longer in the hospital, were treated with neuroleptics for a longer period, and received a larger mean total amount of neuroleptics than patients without tardive dyskinesia. Some studies dealing with younger subjects have identified duration of neuroleptic treatment as a factor in the development of tardive dyskinesia (23–25), whereas others have not (26, 27). It is possible that for our patients with tardive dyskinesia, the larger amounts of neuroleptic medication reflect the longer duration of treatment with these medications.

In some studies (12, 25), drug-free periods have been found to be a factor in the development of tardive dyskinesia, but this was not true in our study.

We were also unable to confirm that the prevalence of tardive dyskinesia increased with age. We found that the younger patients (65–75 years) had a higher but not statistically significant prevalence of tardive dyskinesia than the older patients (76–85 years): 43.4% and 26.3%, respectively. This is consistent with the findings reported recently in a patient group similar to ours, in which aging was not found to contribute to a higher prevalence of tardive dyskinesia (5).

We never prescribe prophylactic antiparkinsonian drugs for our patients. Whenever acute extrapyramidal side effects develop, we prefer to reduce the neuroleptic dosage as a first choice, rather than giving antiparkin-

sonian drugs. Even so, we found that patients with tardive dyskinesia received significantly more antiparkinsonian drugs than patients without tardive dyskinesia, indicating that acute extrapyramidal side effects may develop more in patients with tardive dyskinesia than in those without tardive dyskinesia. A possible reason for the greater amounts of antiparkinsonian drugs received by patients with tardive dyskinesia is that these patients received larger amounts of neuroleptics.

Our study confirms the finding that more patients with affective disorders than patients without affective disorders have tardive dyskinesia. Several studies (28–31) have indicated that patients with affective disorders (particularly depressed patients) are more prone to develop tardive dyskinesia than patients in other diagnostic categories. Our study indicates that this holds true even in an elderly psychiatric population. We found that tardive dyskinesia was more prevalent among depressed patients (60.0%) than among patients with primary degenerative dementia (24.5%) or delusional (paranoid) disorder (26.1%). This higher prevalence of tardive dyskinesia in depressed patients does not reflect the duration or total amount of neuroleptic treatment, and it is difficult at present to speculate on the reason for the higher prevalence in these patients.

In summary, tardive dyskinesia developed in 35.4% of elderly psychiatric patients who received neuroleptics for up to 60 months. We found that gender was not a factor in the development of tardive dyskinesia in this aged population. Patients with tardive dyskinesia, however, received neuroleptics for longer periods and in larger amounts than patients without tardive dyskinesia. They also received more antiparkinsonian drugs, indicating that acute extrapyramidal side effects may be precursors of the development of tardive dyskinesia. More patients with affective disorders than patients in other diagnostic categories developed tardive dyskinesia; thus, clinicians should be cautious when prescribing neuroleptics for these patients.

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An Evaluation of the Cleveland Criteria for Inpatient Treatment of Substance Abuse

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***Objective:** This study examined the validity of the Cleveland Admission, Discharge, and Transfer Criteria, a comprehensive system for assigning alcohol- and drug-abusing patients to appropriate levels of care. **Method:** The subjects were 143 alcoholic and cocaine-dependent male patients in an intensive Veterans Administration day treatment program for substance abusers. Patients who should have received inpatient treatment according to the Cleveland criteria were compared with those who were properly "matched" to day treatment according to the criteria. The outcome measures were treatment completion, results of urine toxicology screens, and self-reports of substance use and psychosocial functioning. **Results:** Patients who met the criteria for inpatient care were not more likely to drop out of day hospital treatment, and there was no evidence that they were drinking or using cocaine more frequently during follow-up. Furthermore, they did not appear to be doing worse on any of the other outcome measures, with the exception of psychological status. **Conclusions:** The results suggest that for male substance abusers in the lower socioeconomic levels, the Cleveland criteria may not be effective in differentiating patients who can manage well with day hospital treatment and those who require inpatient treatment.*

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One of the more actively debated questions in the field of substance abuse treatment concerns which patients will benefit most from what type of treatment (1, 2). Much of the attention in this area has been focused on differentiating patients who require inpatient rehabilitation from those who can manage equally well on an outpatient or day treatment basis.

Given the greater expense of inpatient treatment (3, 4), as well as the disruption it may entail for patients and their families, outpatient rehabilitation has been seen as the treatment of choice whenever possible. At the same time, the general feeling has been that patients with more severe substance abuse, current psychiatric comorbidity, or severely dysfunctional living situations probably need inpatient treatment (2, 4, 5).

In an effort to improve the matching of substance abuse patients to various levels of care, Hoffman et al. (6) developed the Cleveland Admission, Discharge, and Transfer Criteria, which provide guidelines for assess-

ing patients in seven areas: acute intoxication/withdrawal, physical complications, psychiatric complications, impairments in certain areas of life, acceptance of treatment, loss of control, and recovery environment. Ratings in each of these areas are used to determine the appropriate level of care, ranging from level I (mutual self-help groups) to level VI (medically managed intensive inpatient unit). According to the Cleveland criteria, patients are in need of inpatient rehabilitation (as opposed to intensive outpatient treatment) when they reach a certain level of severity in one or more of the seven areas, or "dimensions."

Treatment providers, as well as third-party payers, are greatly in need of objective, validated guidelines for appropriate patient placement; hence, the Cleveland criteria have generated considerable interest (1). There is some initial evidence for the validity of the criteria. Clinical observation as well as a number of research studies have shown that substance abusers with poorer social supports and greater severity of psychiatric disorder typically show less improvement and poorer post-treatment outcomes with outpatient care than with inpatient treatment (7). However, the Cleveland criteria have not been empirically validated as a comprehensive system for assigning patients to appropriate treatment modalities.

In this study, our goal was to evaluate the Cleveland criteria for inpatient rehabilitation. As part of a recent study comparing the efficacy and costs of inpatient and

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TABLE 1. Characteristics of 143 Patients With Alcoholism or Cocaine Dependence at Intake Into a Day Treatment Program

Characteristic	All Patients (N=143)		Alcoholic Patients (N=70)		Cocaine-Dependent Patients (N=73)	
	Mean	SD	Mean	SD	Mean	SD
Age (years)	38.86	9.03	43.42	9.15	34.49	6.39
Education (years)	12.16	2.15	12.18	2.46	12.14	1.83
Earnings in past month (dollars)	435.10	566.90	420.00	535.20	449.60	599.20
Duration of regular substance use (years)			19.84	8.82	2.90	3.14
Days of cocaine use in past 30 days	6.17	8.02	0.74	2.36	11.38	8.08
Days of alcohol use in past 30 days	11.24	9.17	15.26	7.91	7.38	8.66
Addiction Severity Index composite score ^a						
Medical	0.32	0.36	0.38	0.38	0.27	0.33
Employment	0.64	0.27	0.60	0.26	0.68	0.28
Alcohol	0.44	0.30	0.62	0.20	0.26	0.27
Drug	0.14	0.12	0.03	0.06	0.24	0.08
Legal	0.08	0.16	0.06	0.16	0.09	0.16
Family/social	0.24	0.22	0.23	0.23	0.26	0.22
Psychological	0.26	0.21	0.28	0.21	0.25	0.21

^aHigher scores indicate greater problem severity.

day hospital rehabilitation for alcohol- and/or cocaine-dependent patients, we had collected data from patients at admission, during treatment, and at the 4- and 7-month points following intake. An initial examination of the admission data suggested that many of the patients in the day treatment program would have been assigned to inpatient treatment if the Cleveland criteria had been used to match patients to treatments. This group of patients, therefore, would be considered "mismatched" to the day treatment level of care and would be expected to have a higher dropout rate, less improvement, and poorer outcomes than patients treated in the same program who were considered appropriate, or "matched," to that level of care. If these patients did not have worse outcomes, however, it would be difficult to argue that they needed more intensive treatment. The study was thus a test of the validity of the Cleveland criteria for assigning patients to medically supervised intensive inpatient treatment (level V) rather than intensive outpatient treatment (level IV).

METHOD

The subjects were 143 male alcoholic (N=70) or cocaine-dependent (N=73) veterans who were patients in an intensive day treatment program for substance abusers. Patients were not admitted to this program if they were judged by the program physician to have medical or psychiatric problems severe enough to warrant inpatient treatment. In addition, 3% of the subjects who were initially deemed appropriate for day treatment were excluded from participation in the study because of serious medical problems, and 12% were eliminated because of psychiatric problems such as a history of psychosis or dementia.

Of the 143 subjects in the study, 86.7% (N=124) were black and 13.3% (N=19) were white; 23.8% (N=34) were married, and 46.2% (N=66) had worked fewer than 5 days in the month preceding intake. Addi-

tional information on the patients is presented in table 1. For the most part, the alcoholic and cocaine-dependent patients were comparable, with a few notable exceptions. The alcoholic patients were older, a higher percentage of them were white (24.6% versus 2.8%), and they reported more years of regular use of their substance of abuse than the cocaine-dependent patients.

Data Collection

At intake or during the first week of treatment, the subjects were given the following structured interviews, counselors' ratings, and patients' self-report instruments.

Addiction Severity Index (8). The Addiction Severity Index is a 45- to 60-minute structured interview, administered by a trained technician, that assesses degree of problem severity in seven areas in which substance abusers typically experience difficulties, including drug and alcohol use, criminal activity, employment, family/social functioning, and psychological health. The Addiction Severity Index is widely used in addictions treatment research and has been shown to be a reliable and valid instrument (9-11). In this study, baseline and follow-up data were gathered with the Addiction Severity Index.

National Institute of Mental Health Diagnostic Interview Schedule (DIS) (12). DSM-III-R axis I psychiatric diagnoses were obtained with this structured research interview.

Hopkins Symptom Checklist-90 (SCL-90) (13). This widely used and well-validated self-report instrument was used to assess patients' subjective level of emotional distress. The mean score was 70.52 (SD=60.02), with a range of 0-231.

Rating scale for resistance to treatment. During the first week of treatment, counselors rated patients on their degree of denial and resistance to treatment on an instrument with nine items taken from the Resistance to Treatment scale (which has six items) and the Resistance to Continuing Care scale (which has five items)

developed by Mee-Lee and Hoffmann (14). The internal consistency (α) of the scale was 0.93. The mean score was 13.0 (range=0–24); higher scores indicate greater acceptance of treatment.

Rating scale for social/family environmental status. During the first week of treatment, counselors rated the degree of support for sobriety and recovery in the patient's family/social network. The seven items were from the nine-item Social/Family Environmental Status scale, also developed by Mee-Lee and Hoffmann (14) for use with the Cleveland criteria. The α for this scale was 0.83. The mean score was 9.1 (range=1–21); higher scores indicate greater environmental support for sobriety.

Operationalizing the Cleveland Criteria

According to the Cleveland criteria, substance abusers should be referred to inpatient treatment if they reach a certain level of severity on any of the seven dimensions (6). The first two dimensions involve assessing the severity of the patient's withdrawal and/or physical complications. Because patients who have problems in these areas that are serious enough to warrant inpatient treatment were not referred to the intensive outpatient program, no attempt was made to evaluate these two dimensions.

The five dimensions of the Cleveland criteria on which patients were rated, the instruments used to rate patients on each of them, and the number of patients who qualified for inpatient treatment on each dimension according to the criteria were as follows.

Dimension 3: psychiatric complications. The Cleveland criteria propose that a patient requires inpatient care if he or she is currently depressed, suffering from a major personal loss, overly hostile, or displaying extreme emotions. Patients were rated as meeting the criteria for this dimension if they had current major depression (according to the DIS) or extreme symptom severity (SCL-90 score greater than 120) (N=36).

Dimension 4: life area impairments. The Cleveland criteria propose that patients who are violent when intoxicated or who have a legal or Employee Assistance Program mandate for comprehensive rehabilitation require inpatient care. Patients were rated as meeting the criteria for this dimension if they reported violent behavior in the preceding 30 days (Addiction Severity Index) (N=16).

Dimension 5: treatment acceptance/resistance. The Cleveland criteria propose that significant denial and minimization of the substance abuse problem preclude compliance with a lower level of care than inpatient treatment. Patients were rated as meeting the criteria for this dimension if they were rated by counselors as high on denial and treatment resistance (score of less than 10 on the scale for treatment acceptance/resistance) (N=30).

Dimension 6: loss of control/relapse crisis. The Cleveland criteria propose that patients who cannot remain substance free for at least 5 days or who require con-

tinuous use in order to function require inpatient care. Patients were rated as meeting the criteria for this dimension if they reported fewer than 5 days of abstinence (alcoholic patients) or fewer than 10 days of abstinence (cocaine-dependent patients) in the preceding 30 days or reported no abstinent periods of 30 days or more since beginning alcohol/drug use (all data from the Addiction Severity Index) (N=17).

Dimension 7: recovery environment. The Cleveland criteria propose that patients with seriously impaired social, family, or occupational functioning, or those with family members who are not supportive of treatment or who will undermine it in some way, require inpatient care. Patients were rated as meeting the criteria for this dimension if they were typically unemployed or had had no paid work days in the preceding 30 days (Addiction Severity Index), reported more than 9 days of family conflicts in the preceding 30 days or rated their family problems as severe (Addiction Severity Index), or were rated by their counselors as having a social environment not supportive of sobriety (rating of less than 7 on the scale for social/family environmental status) (N=69).

Treatment

After the baseline assessments, the subjects entered an intensive outpatient day treatment program that ran for 27 hours per week. The program generally lasted 4 weeks, although some patients dropped out and others stayed for up to 6 weeks. The program was focused on overcoming the patient's denial, helping the patient learn to cope with everyday problems and stresses, and teaching the patient about cues to relapse. Treatment consisted of 1) supervised milieu therapy, 2) group therapy with a cognitive-behavioral orientation, 3) education sessions three times per week covering information on the biopsychosocial aspects of addiction in a lecture/discussion format, 4) supervised group recreation weekly, and 5) family therapy with a social worker who had a master's degree. Individual counseling was also available as needed. Supervised urine drug screens were performed weekly, and patients were required to participate in at least three Alcoholics Anonymous or Narcotics Anonymous group meetings per week and to obtain a sponsor from the group.

Assessment of Outcome

Outcomes were assessed at 4 and 7 months with Addiction Severity Index composite scores, Addiction Severity Index self-reports of alcohol and cocaine use in the previous 30 days, and results of urine toxicology screens (cocaine patients only). The Addiction Severity Index composite scores are factor-like scores that assess severity of problems in seven separate areas (i.e., alcohol, drugs, medical, employment, legal, family/social, and psychological). The composite scores have a possible range of 0.00–1.00, with higher scores indicating greater problem severity; they have been shown to have

high reliability and good concurrent and predictive validity (9–11).

The standard Addiction Severity Index was administered only to subjects who could be interviewed within 6 weeks of their follow-up date, ranging from 2 weeks before follow-up to 4 weeks after the target date. Those who missed their targeted time frame but could be assessed at a later date were interviewed with an abbreviated form of the Addiction Severity Index ("retrospective" Addiction Severity Index) that yields days of substance use but not the composite scores. Prior to the analyses, the self-reports of alcohol and cocaine use were log transformed to normalize the distributions. However, the untransformed values are presented in the tables for ease of interpretation.

RESULTS

Of the 143 patients assessed at intake, 35 did not meet any of the Cleveland criteria for inpatient care, 55 met one of the criteria for inpatient care, 35 met two criteria, 14 met three, and four met four criteria. According to the criteria, therefore, 108 patients (58 alcoholic and 50 cocaine dependent) should have been assigned to inpatient rehabilitation rather than intensive day treatment. The outcomes of these patients were contrasted with the outcomes of the other 35 patients (12 alcoholic and 23 cocaine dependent) who were correctly matched to intensive day treatment according to the criteria.

Follow-up information from the Addiction Severity Index was available for 87% ($N=124$) of the patients at 4 months and 80% ($N=114$) at 7 months. Complete Addiction Severity Index data from the baseline and the two follow-up assessments were available for approximately 75% of the subjects (when any of the items making up a composite are left blank, the subject does not receive a composite score in that area). The follow-up rate was slightly higher among patients who were properly matched to intensive outpatient treatment (80%) than among those who met criteria for inpatient treatment (72%), although this difference was not statistically significant ($\chi^2=0.73$, $df=1$, $p>0.30$). Reports of number of days of alcohol or cocaine use from retrospective Addiction Severity Indexes were also available for four more patients at 4 months and 15 more at 7 months, which raised the follow-up rates to 89% at 4 months and 91% at 7 months. Follow-up urine toxicology data were available for 66% of the cocaine patients at 4 months and 58% at 7 months.

In terms of treatment participation, there were only slight differences between the groups. Those who qualified for inpatient care spent as many days in the program as those correctly matched to intensive day treatment (17.4 and 17.9 days, respectively; $t=-0.06$, $df=141$, $p>0.95$). A somewhat lower percentage of those who qualified for inpatient care completed the program (68.5% versus 74.3%), and they were also less likely to continue with aftercare (60.2% versus 65.7%), but

these differences were also not significant (for each measure, $\chi^2<0.42$, $df=1$, $p>0.50$).

Patients who qualified for inpatient care were contrasted with those who were correctly matched to intensive outpatient treatment on severity of psychosocial problems during follow-up, as represented by Addiction Severity Index medical, employment, legal, family/social, and psychological composite scores. The data were analyzed in repeated measures analyses of covariance (ANCOVA) with treatment criteria met (inpatient versus outpatient) as the grouping factor, baseline Addiction Severity Index composite score as the covariate, and Addiction Severity Index follow-up composite scores at 4 and 7 months as the repeated factor. Separate ANCOVAs were performed for each Addiction Severity Index composite score. Type of patient (cocaine dependent versus alcoholic) was also originally included as a grouping factor. However, none of the main effects or interactions that involved this factor approached significance, which indicated that the two types of patients could be combined.

The mean Addiction Severity Index composite scores for each group at baseline and at the two follow-ups are presented in table 2. After problem severity at baseline was controlled for, patients who qualified for inpatient treatment had significantly greater severity of psychological problems during follow-up. Although patients who qualified for inpatient treatment also had higher composite scores on the other four psychosocial problem severity composite measures of the Addiction Severity Index at 4 and 7 months, the differences between the groups were generally small, and none reached statistical significance. There were no significant main effects for the repeated factor with any of the Addiction Severity Index composite scores or significant Group by Time interactions, which indicates that the results in each group were stable over the two follow-up periods.

Data on alcohol and drug use and problem severity were also analyzed in repeated measures ANCOVAs. Separate analyses were done for the alcoholic and cocaine-dependent patients. For the alcoholic patients, the outcome measures were Addiction Severity Index alcohol composite score and number of days of alcohol use in the preceding 30 days at each follow-up point. The outcome measures for the cocaine patients were Addiction Severity Index drug composite score and number of days of cocaine use in the preceding 30 days. As in the previous analyses, the covariates were the baseline scores on each of the outcome measures, and the grouping factor was treatment criteria met (inpatient versus outpatient).

The results of these analyses are presented in table 3. Among both alcohol and cocaine patients, there were no significant differences between those meeting criteria for inpatient care and those correctly matched to intensive outpatient treatment on any of the measures of alcohol or drug use/problem severity during follow-up (all F values <0.60 , $p>0.45$). Once again, there were no significant main effects for the repeated factor or

TABLE 2. Psychosocial Problem Severity Scores on the Addiction Severity Index of Patients Meeting the Cleveland Criteria for Intensive Outpatient or Inpatient Treatment^a

Outcome Measure ^b /Group	Severity Score ^c					
	Baseline		4-Month Follow-Up		7-Month Follow-Up	
	Mean	SD	Mean	SD	Mean	SD
Medical						
Patients meeting outpatient criteria (N=28)	0.13	0.24	0.19	0.25	0.11	0.22
Patients meeting inpatient criteria (N=76)	0.37	0.35	0.27	0.36	0.31	0.37
Employment						
Patients meeting outpatient criteria (N=28)	0.58	0.26	0.58	0.32	0.58	0.32
Patients meeting inpatient criteria (N=74)	0.66	0.27	0.62	0.27	0.63	0.29
Legal						
Patients meeting outpatient criteria (N=27)	0.00	0.00	0.02	0.09	0.00	0.01
Patients meeting inpatient criteria (N=78)	0.09	0.17	0.04	0.13	0.02	0.08
Family/social						
Patients meeting outpatient criteria (N=27)	0.12	0.13	0.06	0.10	0.07	0.13
Patients meeting inpatient criteria (N=75)	0.29	0.23	0.13	0.20	0.15	0.21
Psychological ^d						
Patients meeting outpatient criteria (N=26)	0.12	0.17	0.03	0.08	0.01	0.03
Patients meeting inpatient criteria (N=72)	0.32	0.21	0.16	0.21	0.14	0.20

^aAll patients received intensive outpatient treatment.^bComposite score on the Addiction Severity Index.^cHigher scores indicate greater problem severity. Unadjusted outcome scores are presented.^dSignificant difference between groups ($F=4.78$ $df=1, 95$, $p=0.03$).**TABLE 3. Alcohol and Drug Use According to the Addiction Severity Index by Patients Meeting the Cleveland Criteria for Intensive Outpatient or Inpatient Treatment^a**

Outcome Measure/Group	Alcohol and Drug Use ^b					
	Baseline		4-Month Follow-Up		7-Month Follow-Up	
	Mean	SD	Mean	SD	Mean	SD
Alcoholic patients						
Alcohol composite score						
Patients meeting outpatient criteria (N=11)	0.55	0.20	0.09	0.08	0.09	0.09
Patients meeting inpatient criteria (N=41)	0.66	0.19	0.14	0.19	0.13	0.23
Days of alcohol use in past 30 days						
Patients meeting outpatient criteria (N=11)	14.36	8.03	0.09	0.32	2.09	5.97
Patients meeting inpatient criteria (N=42)	16.10	8.00	1.71	4.94	2.67	6.87
Cocaine-dependent patients						
Drug composite score						
Patients meeting outpatient criteria (N=16)	0.22	0.06	0.06	0.08	0.08	0.09
Patients meeting inpatient criteria (N=33)	0.25	0.07	0.09	0.10	0.09	0.10
Days of cocaine use in past 30 days						
Patients meeting outpatient criteria (N=17)	9.24	5.53	1.94	4.99	2.53	5.68
Patients meeting inpatient criteria (N=36)	12.06	8.60	1.67	4.62	1.67	5.52

^aAll patients received intensive outpatient treatment.^bHigher scores indicate greater problem severity. Unadjusted outcome scores are presented. All differences between groups, time effects, and the Group by Time interactions were nonsignificant.

significant Group by Time interactions, which indicates that the substance use results in each group were stable over the two follow-up periods. With the days-of-use measures, the analyses were repeated with data from the retrospective Addiction Severity Indexes included. With this larger sample, there were again no differences among the alcoholic or cocaine-dependent patients between those who met the criteria for inpatient treatment and those correctly matched to outpatient care.

The urine toxicology results are presented in table 4. At both the 4-month and 7-month follow-up points, there were no differences between cocaine-dependent

patients qualifying for inpatient treatment and those correctly matched to intensive outpatient care in the percentage with urine samples positive for cocaine or other drugs. At 4 months, about 32% of the patients had urine samples positive for cocaine, and about 12% had samples positive for other drugs. At 7 months, about 45% had samples positive for cocaine, while less than 5% had samples positive for other drugs. Although the overall follow-up rates for urine toxicology data were not particularly high, it should be noted that the percentage followed up was actually higher among patients qualifying for inpatient treatment, particularly

TABLE 4. Urine Toxicology Results for Cocaine Patients Meeting the Cleveland Criteria for Intensive Outpatient or Inpatient Treatment^a

Drug/Group	4-Month Follow-Up				7-Month Follow-Up			
	Patients Tested		Patients Cocaine Positive		Patients Tested		Patients Cocaine Positive	
	N	%	N	%	N	%	N	%
Cocaine								
Patients meeting outpatient criteria (N=23)	9	39.1	3	33.3	13	56.5	6	46.2
Patients meeting inpatient criteria (N=50)	39	78.0	12	30.8	29	58.0	13	44.8
Other								
Patients meeting outpatient criteria (N=23)	9	39.1	1	11.1	13	56.5	0	0.0
Patients meeting inpatient criteria (N=50)	39	78.0	5	12.8	29	58.0	1	3.4

^aAll differences between groups were nonsignificant.

at 4 months. This suggests that the lack of difference between the groups was not due to a greater rate of missing urine toxicology data from patients meeting the criteria for inpatient care.

While the authors of the Cleveland criteria specify that patients need only qualify on one dimension to be referred to inpatient care, it is possible that somewhat more stringent guidelines would be more effective. We divided the patients on the basis of whether they met the criteria for inpatient care on *two or more* of the dimensions of the Cleveland criteria (N=53). We then compared the same group of patients who were correctly matched to intensive outpatient care (N=35) to this subgroup of 53 patients who were mismatched on the basis of ratings on two or more dimensions. The data were then analyzed with the repeated measures ANCOVA procedure we have described.

Again, there was little evidence that those who should have received inpatient care did any worse at the follow-ups. These patients did have significantly higher Addiction Severity Index composite scores on the family/social ($F=4.76$, $df=1$, 57 , $p<0.03$) and psychological ($F=9.12$, $df=1$, 53 , $p<0.01$) measures during follow-up. However, they did not have higher follow-up Addiction Severity Index medical, employment, or legal composite scores. Among the alcoholic patients, there were no differences in Addiction Severity Index alcohol composite scores or days of alcohol use between those qualifying for inpatient treatment and those properly matched to intensive outpatient care. Among the cocaine-dependent patients, there were no differences between the groups on Addiction Severity Index drug composite scores, days of cocaine use, or urine toxicology results. (The tables presenting the results of these analyses are available from the first author on request.)

Each of the five dimensions of the Cleveland criteria was also evaluated separately in an effort to determine whether one of these might be particularly predictive of poorer performance in day treatment. There was some evidence that patients who qualified for inpatient treatment on dimension 3 (psychiatric complications) or dimension 7 (recovery environment) were experiencing greater family and psychological difficulties during follow-up, as measured by Addiction Severity Index composite scores. Otherwise, there were no clear relation-

ships between any single Cleveland criterion and Addiction Severity Index outcome composite scores, reports of frequency of alcohol or cocaine use, or urine toxicology results during follow-up. (The tables presenting the results of these analyses are also available from the first author on request.)

DISCUSSION

Alcohol- and cocaine-abusing patients who were treated in an intensive outpatient program, but who qualified for inpatient treatment according to the Cleveland Admission, Discharge, and Transfer Criteria, were contrasted with other patients from the same program who were properly matched to intensive outpatient care according to the criteria. Surprisingly, there was little evidence that those who met the criteria for inpatient care were more likely to drop out of outpatient treatment and no evidence that they were drinking or using cocaine more frequently during either the 4- or 7-month follow-up. Furthermore, there was not much evidence to suggest that they were doing worse on any of the other outcome measures, with the exception of psychological status. Even this difference would not have been significant if a Bonferroni correction had been used to adjust the alpha level for the number of comparisons made.

These results suggest that the Cleveland criteria may not be particularly effective in differentiating those who can manage well with intensive outpatient treatment and those who require inpatient treatment for substance abuse. One reason for this may be that the criteria for inpatient treatment are overinclusive. Almost 75% of the patients in the intensive outpatient program met the requirements for inpatient treatment on one or more of the dimensions of the criteria as they were operationalized in this study. Making the criteria for inpatient treatment more restrictive might better differentiate patients who will not do well in outpatient modalities. However, simply requiring that patients meet criteria for inpatient care on more than one dimension did not result in much better identification of patients who did not do well in intensive outpatient treatment.

Several other explanations for these unexpected re-

sults should be considered. First, it is conceivable that the Cleveland criteria for inpatient care were not operationalized properly. While most of the dimensions are clearly spelled out by the authors, others are not as consistently clear as they might be. This was particularly true of dimension 3 (psychiatric complications) and dimension 6 (loss of control/relapse crisis). Although considerable care was taken to ensure that the criteria were represented accurately, it is possible that one or more dimensions were not operationalized in the manner intended by the authors of the Cleveland criteria.

Another possibility is that the Cleveland criteria do not apply to this population of male veterans of lower socioeconomic status with alcohol and cocaine problems. The Cleveland criteria, as currently written, may be more effective with other patient groups, such as middle-class, insured patients who are typically seen in private settings. Certain dimensions of the criteria may also be more or less valid with different groups of patients.

Finally, the Cleveland criteria for inpatient treatment are based on the assumption that patients with more severe symptoms require inpatient care because 1) day hospital or intensive outpatient environments do not have the requisite services to deal effectively with these problems, and 2) inpatient treatment has the appropriate services. However, our intensive day treatment program may have provided considerably more services than the typical intensive outpatient program envisioned by the authors of the Cleveland criteria. In fact, separate studies of this issue have shown that this day hospital program offers very similar types and amounts of treatment services in comparison with our 28-day inpatient program (A.I. Alterman and A.T. McLellan, unpublished manuscript). If the nature and amount of care provided in day hospital and inpatient programs are similar, then it is reasonable to expect the results that were obtained in this study.

In conclusion, determining the proper level of care for substance abusers remains a thorny problem. While a comprehensive system for assigning patients to proper treatment would certainly be welcome, more work appears to be needed as part of the process of "fine-tuning" and validating the Cleveland criteria. Moreover, even if criteria for inpatient rehabilitation of patients with substance abuse were successfully developed for one patient population, it is possible that they would have to be altered or adapted in order to be workable

with other patient populations. Therefore, additional studies with different patient populations and perhaps different types of inpatient and day treatment programs will be required to evaluate fully the Cleveland criteria and any other system for the assignment of patients to appropriate levels of care.

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Mental Health Status and Community Adjustment After Treatment in a Residential Treatment Program for Homeless Veterans

Catherine Leda, M.S.N., M.P.H., and Robert Rosenheck, M.D.

***Objective:** An uncontrolled outcome study was conducted to examine clinical improvement and the relationship of psychiatric and substance abuse problems, community adjustment, and housing status among homeless veterans who participated in a multisite residential treatment program. **Method:** The study was performed at three U.S. Department of Veterans Affairs medical centers in Florida, Ohio, and California. Baseline, discharge, and 3-month postdischarge follow-up data were collected for 255 veterans admitted to the Domiciliary Care for Homeless Veterans Program. Multiple dimensions of outcome were examined, including psychiatric symptoms, alcohol abuse, drug abuse, social contacts, income, employment, and housing. **Results:** Program participation was found to be associated with improvement in all areas of mental health and community adjustment. Improvement in psychiatric symptoms was associated with superior housing outcomes and improvement in community adjustment. When correlates of improvement in alcohol and drug abuse were examined, only one of eight possible relationships was found to be significant: improvement in alcohol problems was positively associated with improvement in employment. **Conclusions:** Homeless mentally ill veterans derive clear benefits from participation in a multidimensional residential treatment program. Improvement in mental health problems, however, is weakly linked to improvement in other areas, suggesting that treatment programs may have to attend separately to multiple domains of life adjustment.*

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During the 1980s the plight of the homeless mentally ill became an increasing focus of public attention and concern (1), a concern that was supported by a series of rigorously conducted community studies that demonstrated an exceptionally high prevalence of psychiatric and substance abuse disorders among the urban homeless (2-4). Although these studies did not provide a definitive explanation for the increased numbers and visibility of the homeless mentally ill across the country, most authorities agreed that the growth in urban poverty and the decline in the availability of affordable housing in most cities left people with psychiatric and substance abuse disorders at particularly high risk

for homelessness (5, 6). Psychiatric symptoms, substance abuse, social dysfunction, and lack of social supports were all identified as placing the mentally ill at special risk for homelessness (5, 6). Indeed, because of the presumed relationship between mental illness and vulnerability to homelessness, clinicians and program planners (1, 7) urged that specialized rehabilitation programs for the homeless mentally ill offer a combination of mental health services, housing assistance, and social rehabilitation services.

Scholarly attention has recently shifted from a primary focus on studying the psychiatric epidemiology of the homeless to evaluating approaches to their treatment (8). Although only a handful of outcome studies have been published (9-11), all have suggested that participation in specialized clinical programs can facilitate movement of the chronically mentally ill out of homelessness. Two premises about this population on which many of these clinical programs are based are that 1) mental illness, social dysfunction, and homelessness are related problems that exacerbate one another and 2) successful clinical intervention must target all of these problem areas. It follows that outcome studies of the homeless mentally ill should assess improvement in multiple domains.

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TABLE 1. Baseline and Discharge Characteristics of 255 Homeless Veterans Reinterviewed 3 Months After Residential Treatment

Variable	N	%
Baseline characteristics		
Duration of current episode of homelessness		
At risk for homelessness ^a	14	5.5
<1 month	60	23.5
1-5 months	106	41.6
6-11 months	38	14.9
12-23 months	23	9.0
>23 months	14	5.5
Days of employment in 30 days before admission		
0	185	72.5
1-19	58	22.7
>19	12	4.7
Clinical psychiatric disorders (DSM-III-R) ^b		
Schizophrenia	7	2.7
Bipolar disorder	8	3.1
PTSD	23	9.0
Depressive disorder	55	21.6
Adjustment disorder	60	23.5
Drug abuse/dependency	105	41.2
Alcohol abuse/dependency	163	63.9
Alcohol and/or drug abuse/dependency	206	80.8
Discharge characteristics		
Mode of discharge		
Successfully completed program	98	38.4
Was asked to leave	69	27.1
Left by choice (against medical advice)	74	29.0
Other	14	5.5
Living arrangement		
Apartment, room, or house	134	52.5
Institution	44	17.3
Shelter or outdoors	15	5.9
Other	15	5.9
Unknown	47	18.4
Employment status (N=254)		
Employed	100	39.4
Retired or disabled	32	12.6
Unemployed	98	38.6
Other	24	9.4

^aEither housing was in imminent jeopardy or subject was institutionalized before admission but had no housing arrangements at the time of discharge.

^bSome veterans had more than one psychiatric diagnosis.

In this paper we examine the relationship of psychiatric and substance abuse problems, community adjustment, and housing status among homeless veterans who participated in a multisite study by the U.S. Department of Veterans Affairs (VA) Domiciliary Care for Homeless Veterans Program. The Domiciliary Care for Homeless Veterans Program is a multidimensional, time-limited residential treatment program for homeless veterans that addresses both personal and practical aspects of community adjustment (12, 13).

In this investigation we explored three hypotheses: 1) that severe psychiatric symptoms and substance abuse problems at admission would be associated with community adjustment problems and more prolonged homelessness, 2) that improvement in both mental health and community adjustment would be noted at follow-up, and 3) that improvement in psychiatric symptoms and substance abuse problems in particular would be associated with improvement in community

adjustment and housing status. We thus examined the impact of residential treatment and explored the relationship between mental health problems and community adjustment.

METHOD

In November 1987 the VA established the Domiciliary Care for Homeless Veterans Program at 20 VA medical centers. Each site has 25-75 beds and is staffed by a multidisciplinary professional team that provides seriously ill homeless veterans with medical and psychiatric treatment and with social-vocational rehabilitation services (12). All veterans with substance abuse problems are required to participate in substance abuse treatment, as well as group therapy and individual counseling. All sites offer prevocational and work-for-pay rehabilitation programs and maintain an active therapeutic community (13).

Of the 20 sites in the program, three were invited to participate in a descriptive outcome study: those located at the VA medical centers in Bay Pines, Fla., Cleveland, Ohio, and Palo Alto, Calif. These sites were selected because 1) they were among the first to have fully implemented programs, 2) they represent diverse regions of the country, and 3) they expressed interest in undertaking a demanding follow-up study. Although few objective operational data on the three sites are available, site visits indicated that one site emphasizes a cognitive-behavioral approach, another emphasizes vocational rehabilitation, and the third site stresses case management. Every first-time participant at each site during a 9-month period was invited to join the study. Of the 421 veterans so invited, 383 (91%) agreed to participate.

Data Collection

Data collection involved a three-step process. First, baseline data were obtained at the time of the veteran's first contact with the program and within 10 days of admission. Second, at the time of discharge, each veteran's primary clinician recorded pertinent data on the veteran's participation in the program. Finally, follow-up data on 255 subjects were collected through a structured interview with a research assistant 3 months after discharge. At one of the sites a few of the follow-up interviews were conducted by a clinician because the research assistant was not available. Because some veterans had relocated some distance from the VA medical centers after discharge, 70 (27.5%) of the veterans were interviewed over the telephone at follow-up, and the remaining 185 (72.5%) were interviewed in person.

Baseline data documented demographic and military service characteristics and the duration of the veteran's current episode of homelessness (time without a fixed, regular, and adequate nighttime residence). Duration of homelessness was evaluated with a six-level ordinal variable (see table 1). Psychiatric, alcohol, and drug prob-

lems were assessed by using selected items from the Addiction Severity Index (14), which were organized into composite indexes of alcohol problems, drug problems, and psychiatric problems by using the methods for combination suggested by McLellan et al. (unpublished manual of P.L. McGahan et al.), although slight modifications were made in the measure of psychiatric problems. The Addiction Severity Index has been shown to be reliable and valid in other studies (15), although tests of reliability and validity specific to this study were not performed.

The data collected at baseline also included measures of social contact, employment status, and current income. Frequency of social contact was expressed as a social contact index, a weighted sum of the frequency of face-to-face contacts with individuals that the veteran reported feeling close to in eight relationship categories. To calculate the social contact index, the number of close relationships was multiplied by the veteran's estimate of the frequency of contacts. Employment was measured on an ordinal scale, where 0 indicated the veteran did not work for pay at all during the 30 days before admission to the program, 1 represented working 1–19 days (part-time), and 2 represented working 20 or more days (full-time). Income was calculated by taking the sum of all reported sources of income in the 30 days before admission.

At discharge, length of stay and the mode of discharge from the program (successfully completed program, asked to leave for rule violation, left prematurely by choice, or other reason) were recorded. Postdischarge housing, employment, and health care arrangements were also recorded.

At the 3-month follow-up interview, measures equivalent to those used at baseline were completed. A detailed residential history was also taken; the veteran was asked to recall, for the 90 days after discharge, the number of nights spent in each of 11 types of living arrangements. These living arrangements were then collapsed to yield three categories: 1) number of nights housed, 2) number of nights institutionalized, and 3) number of nights homeless. Nights homeless was defined as the number of nights the veteran slept outdoors, in a shelter for the homeless, or in a vehicle. From these three categories a housing index was created. The housing index was a weighted sum; the number of nights housed was multiplied by 2, the number of nights institutionalized was multiplied by 1, and the number of nights homeless was multiplied by 0. This scoring system was based on the view that being domiciled in an apartment, room, or house was superior to being institutionalized and that both were superior to being homeless.

Subjects

Three months after discharge, 255 (66.6%) of the veterans in the cohort were located and interviewed, 58 (15.1%) were located but could not be interviewed, two (0.5%) were known to have died, and 68 (17.8%)

could not be located. The veterans reinterviewed 3 months after discharge were not significantly different from the veterans who were not interviewed in age, ethnicity, educational level, employment history, criminal history, duration of homelessness, most clinical diagnostic categories, mode of discharge from the program, and housing and employment status at discharge. However, there were significant differences between these groups in three admission variables and two discharge variables. At admission those who were reinterviewed were more likely to have never been married (36% versus 23%; $\chi^2=5.36$, $df=1$, $p=0.02$), more likely to have serious medical problems (67% versus 51%; $\chi^2=8.41$, $df=1$, $p=0.004$), and less likely to be clinically diagnosed with both psychiatric and substance abuse diagnoses (28% versus 41%; $\chi^2=6.22$, $df=1$, $p=0.01$). At discharge those who were reinterviewed were more likely to have been discharged to another institutional setting (23% versus 11%; $\chi^2=7.45$, $df=1$, $p=0.006$) and more likely to have had follow-up arrangements for health care treatment (90% versus 81%; $\chi^2=6.27$, $df=1$, $p=0.01$). Although only 66.6% of the cohort were reinterviewed, they appear to be a reasonably representative subgroup of the veterans who participated in the study.

The 255 veterans who were reinterviewed 3 months after discharge had a mean age of 40.1 years ($SD=9.6$), and 96.9% were male ($N=247$). The majority (56.9%) were white ($N=145$), 38.8% were black ($N=99$), 3.1% were Hispanic ($N=8$), and 1.2% were Native American or Asian ($N=3$). Only 2.4% were married ($N=6$); 62.0% were widowed, separated, or divorced ($N=158$), and 35.7% had never married ($N=91$). Almost 85% had completed at least 12 years of education ($N=213$), and in the 30 days before admission the majority (72.5%, $N=185$) had not worked at all. Eighty percent had been homeless for less than 12 months (table 1). The clinical psychiatric assessments conducted at admission by mental health clinicians indicated that 80.8% of the veterans met the criteria for an axis I *DSM-III-R* diagnosis of drug and/or alcohol abuse/dependency (table 1).

Analysis

Analyses were conducted in three stages. First, the Pearson product-moment correlation (r) was used to determine the correlation between mental health and community adjustment measures at admission. Next, t tests were used to determine the significance of differences between baseline and follow-up measures. Finally, improvement in clinical and community adjustment was determined by using standardized residual scores of the regression of follow-up scores on baseline scores. Pearson's r was then used to determine the correlation of improvement in mental health and community adjustment domains. All analyses were conducted for each site individually and for pooled data from all sites. The tables present pooled data and findings that were statistically significant at two or more sites ($p<0.05$).

TABLE 2. Correlation of Baseline Mental Health With Duration of Homelessness and Baseline Community Adjustment for 255 Homeless Veterans

Baseline Composite Measure From Addiction Severity Index	Duration of Homelessness		Baseline Community Adjustment Measure					
	r ^a	p	Social Contact		Income		Employment	
			r ^a	p	r ^a	p	r ^a	p
Psychiatric problems	0.07	n.s.	-0.07	n.s.	0.11	n.s.	-0.17	0.006
Alcohol problems	0.07	n.s.	0.15	0.02	-0.01	n.s.	0.02	n.s.
Drug problems	0.01	n.s.	0.21	0.001	0.07	n.s.	-0.08	n.s.

^adf=253.**TABLE 3. Changes in Mental Health and Community Adjustment for 255 Homeless Veterans From Admission to 3 Months After Residential Treatment**

Measure	Admission		Follow-Up		Difference		Analysis	
	Mean	SD	Mean	SD	Mean	SD	t (df=254)	p
Addiction Severity Index composite								
Psychiatric problems	1.183	0.764	0.659	0.716	-0.524	0.831	-10.06	0.0001 ^a
Alcohol problems	0.210	0.216	0.176	0.225	-0.345	0.245	-2.60	0.03
Drug problems	0.062	0.079	0.045	0.079	-0.017	0.080	-3.29	0.001
Community adjustment								
Social contact index ^b	196.514	235.181	367.161	266.830	170.647	309.840	8.79	0.0001 ^a
Monthly income (dollars)	255.00	628.64	725.00	854.84	470.00	1060.68	7.08	0.001 ^a
Employment status ^c	0.322	0.560	0.973	0.894	0.651	0.064	10.16	0.001 ^a

^at test results were significant at two or more sites (p<0.05).^bNumber of close relationships multiplied by frequency of contacts.^cDays of paid employment in previous 30 days; 0=0 days, 1=1-19 days, 2=20 or more days.

RESULTS

The mean length of stay in the program for the interviewed veterans was 4.7 months (SD=3.2), and 38.4% were judged to have successfully completed the program (table 1). An additional 27.1% were asked to leave, primarily because of substance use, and 29.0% left against medical advice. At the time of discharge, more than one-half (52.5%) had housing arrangements, and 17.3% were discharged to other institutional settings (see table 1). Almost 40% had plans for employment after discharge.

Table 2 indicates the correlations of the baseline mental health indexes with duration of homelessness and baseline community adjustment. Only three of the 12 correlations were significant. The baseline index of psychiatric symptoms was negatively associated with employment, and the baseline indexes of alcohol and drug abuse were positively correlated with social contact, most likely reflecting the frequent contact of substance-abusing veterans with their "drinking and drugging buddies." Contrary to expectations, no associations were found between any of the baseline mental health indexes and the duration of homelessness or income. In this group psychiatric problems and substance abuse were not strongly associated with poorer community adjustment.

At admission 94.5% of the subjects (N=241) were literally homeless. In contrast, in the 90 days after discharge only 20.8% (N=53) were homeless for even 1 day and only 11.0% (N=28) reported being homeless

for more than 45 days. Furthermore, 83.5% (N=213) were housed for at least 1 day and 66.3% (N=169) reported being housed the majority of the time.

Changes in indexes of mental health and community adjustment are shown in table 3. All measures of mental health problems (psychiatric symptoms, alcohol problems, and drug problems) showed statistically significant reductions, and the most dramatic reduction from admission to follow-up was for psychiatric symptoms.

Significant improvement was also noted for all measures of community adjustment (table 3). Social contact increased, largely because a greater proportion of veterans were having daily contact with spouses or significant others, friends, health care providers, and other family members (data available on request). Monthly income rose substantially, by an average of \$470, primarily because of an increase in employment income, consistent with the significant improvement in employment.

Associations between measures of improvement in mental health problems and measures of improvement in community adjustment and housing are presented in table 4. Improvement in psychiatric symptoms was significantly but weakly associated with improvement in housing and with all three major measures of improvement in community adjustment.

When correlates of improvement in substance abuse were examined (table 4), only one significant relationship was observed: improvement in alcohol problems was positively associated with improvement in employment. No significant relationships were found between

TABLE 4. Correlation of Improvement in Mental Health With Improvement in Housing and Community Adjustment for 255 Homeless Veterans After Discharge From Residential Treatment

Improvement in Composite Measure From Addiction Severity Index ^a	Improvement in Community Adjustment ^a							
	Housing Index		Social Contact		Income		Employment	
	r ^b	p	r ^b	p	r ^b	p	r ^b	p
Psychiatric problems	0.16	0.009	0.16	0.01 ^c	0.18	0.004 ^c	0.29	0.0001 ^c
Alcohol problems	0.03	n.s.	0.01	n.s.	-0.02	n.s.	0.20	0.001 ^c
Drug problems	0.02	n.s.	0.00	n.s.	0.00	n.s.	0.14	n.s.

^aMeasured by residual scores.^bdf=253.^cCorrelations were significant at two or more sites ($p < 0.05$).

improvement in drug problems and improvement in either community adjustment or housing status after discharge.

DISCUSSION

The central finding of this study of homeless mentally ill veterans was that participation in a residential treatment program was associated with improvement in both mental health and community adjustment. Although this was not a controlled outcome study, we believe that the degree of clinical improvement reported here would not have occurred in the absence of this intervention.

Other studies (12) have indicated that, among the homeless, individuals with psychiatric illnesses have more severe community adjustment problems than do others, but that trend did not emerge in our study. This finding suggests 1) that the psychiatric symptoms of a help-seeking clinical population are less severe than those of the general homeless population and 2) that within a chronically mentally ill population psychopathology and community adjustment vary with relative independence (16).

While previous studies have reported improvements in housing status associated with participation in specialized treatment programs for the homeless mentally ill (9-11), those studies have not shown improvement in other domains. To our knowledge this is the first outcome study on the treatment of the homeless mentally ill to indicate improvement in multiple areas, an important and positive finding in a population known to suffer from multiple problems.

Several methodological limitations, however, require comment. First, this study did not have an experimental design, and as a result the improvements noted cannot be conclusively attributed to treatment. Second, attrition at follow-up was substantial and may have biased the findings. Although few significant differences were found between the veterans who were interviewed at follow-up and the veterans who were not, the postdischarge outcomes of those not interviewed are unknown and may have been poor. Finally, the assessment of substance abuse was based on self-report data alone, which may have resulted in some underreporting. In spite of

these limitations, to our knowledge the findings reported here are the first to address multiple dimensions of outcome among the homeless mentally ill and are generally encouraging.

Although significant, the association between improvement in psychiatric symptoms and improvement in community adjustment was modest. Thus, these data only weakly support the hypothesis that treatment through the Domiciliary Care for Homeless Veterans Program effectively reduces psychiatric symptoms and thereby allows a veteran to resume productive social and vocational roles in the community. It must also be acknowledged that since psychiatric symptoms and community adjustment were measured at the same time, the direction of causality cannot be determined unambiguously. It is possible that social-vocational interventions in the Domiciliary Care for Homeless Veterans Program led first to improved community adjustment, which then resulted in reduced psychiatric symptoms. Most likely, the lines of influence, although weak, run both ways.

We found only one significant association between improvement in substance abuse and improvement in community adjustment. There are several possible explanations for this negative finding. First, improvement in community adjustment among veterans who evidenced improvement in substance abuse might have occurred slowly, and as a result, associations between these domains might not have been apparent only 3 months after discharge from residential treatment. Second, it is possible that some patients who remained dysfunctional because of continued substance abuse did not report the full extent of their substance use in the follow-up interviews.

Our hypothesis that improvement in psychiatric symptoms and substance abuse problems would be consistently associated with improvement in community adjustment and housing status was only weakly supported in this study. Clearly, additional studies are needed to more fully address these important questions. Such studies should, whenever possible, use experimental methods, validate substance abuse through objective means, and collect assessment data from as many domains as possible.

This study suggests a positive impact of participation in a residential treatment program for homeless veter-

ans on multiple clinical and community adjustment domains. It appears that, among the homeless mentally ill, improvement in mental health problems is weakly linked to improvement in other areas and that treatment programs may have to attend separately to multiple domains of life adjustment. The homeless mentally ill are among the least fortunate members of our society. They deserve our best efforts at both understanding and assisting them.

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Sensitivity of Psychiatric Diagnosis Based on the Best Estimate Procedure

Therese A. Kosten, Ph.D., and Bruce J. Rounsaville, M.D.

Objective: A "best estimate" diagnosis is one made by expert clinicians on the basis of diagnostic information from direct interview conducted by another clinician plus information from medical records and from reports of family members. The authors address the question of whether the best estimate procedure can enhance the classification of psychiatric diagnoses of subjects who are interviewed directly. **Method:** Four hundred seventy-five subjects were interviewed directly: 201 opiate-addicted probands who sought treatment from a university-based clinic and 274 of their spouses and/or first-degree relatives. Subjects were interviewed by trained clinical assessors using the Schedule for Affective Disorders and Schizophrenia and classified according to Research Diagnostic Criteria. Two psychologists independently diagnosed the same subjects by applying the best estimate procedure. Lifetime rates of major and minor depressive disorder, antisocial personality, alcoholism, and drug abuse were calculated. The rates of diagnoses made on the basis of direct interviews alone were compared with the rates of diagnoses made according to the best estimate procedure. **Results:** Higher rates of diagnoses of all four disorders were made when the best estimate procedure was applied than when direct interview alone was used; the best estimate procedure also resulted in a minimal rate of false positives. **Conclusions:** The higher rate of diagnoses based on the best estimate procedure may represent an enhancement in the accuracy of psychiatric diagnoses or an increase in erroneous diagnoses. The authors consider the second possibility less likely.

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Accurate classification of psychiatric diagnoses is important for genetic, epidemiologic, and treatment research. Misclassification can lead to erroneous conclusions about the etiology or outcome of psychiatric disorders. Using structured interviews and specific diagnostic criteria (1) provides a good basis for accurate classification of psychiatric diagnoses. However, direct interviews may not be available (e.g., in a family study when a relative cannot be contacted because of death, refusal, or other reasons). Moreover, the data from these interviews may be inaccurate if the subject withholds or provides false information.

To address these problems, psychiatric diagnoses can be obtained by enhancing interview data with informa-

tion from medical records and from reports of family members. Diagnostic information from all these sources are compiled and rated by expert clinicians to yield a "best estimate" diagnosis (2). These clinicians are not involved in the actual interviews of the subjects, including those of their family members. This blind procedure allows for objective evaluation of diagnoses but can lead to disagreements on diagnoses. When this occurs, the cases are reviewed and a consensus is reached. This process increases the cost of the study and raises the question of whether the best estimate procedure provides enough valuable diagnostic information to warrant its increased cost for subjects who are directly interviewed. For subjects who cannot be interviewed, the best estimate procedure has been shown to provide good diagnostic information (2).

The present paper addresses the question of whether the best estimate procedure can enhance the classification of psychiatric diagnoses for subjects who are interviewed directly. Working under the assumption that the best estimate procedure is more accurate than direct interview data because it is based on multiple sources of information, we compared psychiatric diagnoses obtained from direct interview only with diagnoses based on the best estimate procedure. We also assessed the degree to which the direct interview classified a subject

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as having a psychiatric diagnosis when the best estimate procedure did not. The latter may represent either false positive direct interview diagnoses or erroneous classifications of best estimate diagnoses.

METHOD

The 475 subjects in this study were obtained from a large family study of opiate addiction (3). They included 201 opiate-addicted probands who sought treatment from a university-based clinic during the years 1983–1985 and 274 of their spouses and/or first-degree relatives, who were also interviewed directly. All subjects were at least 18 years old and gave informed consent in accordance with the Yale University Human Investigations Committee.

Subjects were interviewed by trained clinical assessors using the Schedule for Affective Disorders and Schizophrenia (SADS) (4) and classified according to Research Diagnostic Criteria (RDC) (5). Family history data were collected by using the family history version of the SADS/RDC. In the present paper, we report the lifetime rates (current or past) of major or minor depressive disorders, antisocial personality, alcoholism, and drug abuse.

Two psychologists independently diagnosed the same subjects by applying the best estimate procedure; they reviewed the data from direct interview, family history reports, and medical records. They discussed the diagnoses on which they disagreed and obtained a consensus on each. The interrater reliability was very good; mean kappa was 0.89 (range=0.62–1.00).

RESULTS

Data obtained from the direct interview were available for all 475 subjects diagnosed according to the best estimate procedure. Additional information from medical records was available for 128 (27%) of these subjects, and additional information from family history reports (i.e., interviews with family members about the subject) was available for 439 (92%) of these subjects. The mean number of family history reports from spouses and/or first degree relatives per subject was 2.2 (SD=2.2).

We calculated the percent of subjects who were given each of the diagnoses according to the best estimate procedure but who were classified as not having the diagnosis according to the direct interview data. These false negative rates are given in table 1. The rate of false negatives for all diagnoses ranged from 7% to 41%. The greatest false negative rate occurred for antisocial personality, and the lowest occurred for drug abuse.

We also calculated the percent of false positive diagnoses—subjects who were given the diagnosis by the direct interview method but not by the best estimate procedure. These data are also given in table 1. Overall, the false positive rates were minimal. Two disorders, alcoholism

TABLE 1. False Negative and False Positive Rates for Psychiatric Diagnoses Based on Direct Interview Only Compared With Diagnoses Based on Best Estimate Procedure

Diagnosis	Number of Subjects	False Negative Rates		Number of Subjects	False Positive Rates	
		N	%		N	%
Depressive disorders	275	57	21	200	3	2
Antisocial personality	194	80	41	281	4	1
Alcoholism	235	56	24	240	0	0
Drug abuse	326	23	7	149	0	0

and drug abuse, had no false positive rate. The other two diagnoses had minimal false positive rates.

We tested the generalizability of the enhanced accuracy of the best estimates with subsamples of the data. First, we compared the diagnoses of subjects for whom family history reports were available (N=439) with those for whom they were not available (N=36). There were no group differences in the false negative rates for the four diagnoses when the direct interview data were compared with the best estimate data (range=0%–5%).

Second, we compared those subjects whose medical records were available (N=128) with those whose records were not available (N=347). There were no group differences for the diagnoses of depressive disorders or drug abuse. However, when the direct interview diagnoses were compared with the best estimate diagnoses, the false negative rate for antisocial personality was 39% and the false negative rate for alcoholism was 33% for the 128 subjects with medical record data. These rates were significantly higher than the rates for the 347 subjects without medical records available, for whom the false negative rate for antisocial personality was 18% ($\chi^2=16.2$, $df=1$, $p<0.01$) and the false negative rate for alcoholism was 15% ($\chi^2=9.6$, $df=1$, $p<0.01$).

Finally, because almost half of the subjects were treatment-seeking opiate addicts, which may have artificially enhanced the agreement between direct interview and best estimate data, we compared the diagnostic agreement between the two procedures for the treatment-seeking probands (N=201) and their family members (N=274). We did not examine the group differences for the diagnosis of drug abuse because the proband group was defined by this diagnosis. There were no differences between the probands and their family members for depressive disorders and alcoholism. However, the false negative rate for antisocial personality was 48% for the probands, compared with 9% for their family members ($\chi^2=70.5$, $df=1$, $p<0.001$).

DISCUSSION

This study shows that when best estimate diagnoses, based on multiple information sources, are compared

with diagnoses made from direct interview only, there are many false negatives and few false positives. The false negative rate was particularly high for antisocial personality, but the rates for the depressive disorders and alcoholism were also high. Among the drug-abusing probands, the higher rate of diagnosis of antisocial personality when the best estimate procedure was applied was particularly striking. However, minimal or no false positives were obtained from the direct interview data compared with the best estimate data. These findings support the utility of making best estimate diagnoses for interviewed subjects.

We had expected that using the best estimate procedure would result in more diagnoses of disorders for which the criteria are based on information that subjects may tend to withhold (6). Our finding that the smallest increase was in the rate of drug abuse diagnoses was undoubtedly due to the fact that family members were aware that the probands were seeking drug abuse treatment. The higher rates of diagnoses of alcohol abuse and, particularly, of antisocial personality, are in line with the concept that interviewees may withhold information related to these disorders but this information can be gained by obtaining family history data and medical record data.

One finding that was particularly striking was the usefulness of including data from medical records in the best estimate diagnoses. The rates of diagnosis of two of the four disorders—alcoholism and antisocial personality—were significantly higher in subjects for whom medical record data were available than in subjects for whom these data were not available. Previous research also shows that medical record data enhance the rate of antisocial personality and alcoholism diagnoses as well as drug abuse diagnoses (7). The probable reason that we did not find this effect with the drug abuse diagnosis was that almost half of the subjects were treatment-seeking opiate addicts, which would make the medical record data somewhat obsolete.

Diagnoses based on family history information, compared with those based on direct interview, result in un-

derreporting of cases (8–10). We have now shown that the direct interview itself may result in underestimates of diagnostic rates. When family history information, along with medical record data, are incorporated into the diagnosis by using the best estimate procedure, the number of positive cases is greatly increased. This increase in diagnoses with the best estimate procedure may represent an enhancement in the accuracy of psychiatric diagnoses if, as we assumed, this procedure is a better standard, or it may reflect an increase in erroneous diagnoses because more errors may occur with greater available information. Although we consider the second possibility less likely, we have no other standard by which we can compare these diagnoses.

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The Relationship Between Personality and *DSM-III* Axis I Disorders in the Population: Results From an Epidemiological Survey

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Objective: The aim of this study was to assess the relationships between specific personality disorders and *DSM-III* axis I conditions in a community sample. **Method:** A total of 810 subjects were examined by psychiatrists in the second stage of the Eastern Baltimore Mental Health Survey, part of the Epidemiological Catchment Area Program of the National Institute of Mental Health. A semistructured examination, the Standardized Psychiatric Examination, was employed to assess axis I and axis II conditions. Scales for compulsive and antisocial personality disorders were derived from *DSM-III* criteria. The relationships between scores on these personality disorder scales and the presence of generalized anxiety disorder, alcohol use disorders (alcohol abuse and alcohol dependence), and simple phobia were evaluated by using logistic regression. **Results:** Higher compulsive personality scores were associated with a greater odds of generalized anxiety disorder and simple phobia but a smaller odds of alcohol use disorders. In contrast, higher antisocial personality scores were associated with a greater odds of alcohol use disorders but a smaller odds of generalized anxiety disorder. There was no relationship between antisocial personality scores and simple phobia. **Conclusions:** Personality disorders have specific relationships to axis I conditions, which suggests different vulnerabilities but also different protective influences.

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D *SM-III* made a fundamental contribution to the study of personality disorders by providing explicit diagnostic criteria for these conditions and clearly distinguishing them from axis I psychiatric disorders (1). Since then, clinical interest in the personality disorders has burgeoned. It has become evident that the personality disorders are not discrete but show considerable overlap with each other (2). In addition, the question has been raised as to whether a categorical or dimensional approach to their characterization is more appropriate (3). More recently, the relationships between the personality disorders and axis I conditions have received considerable interest.

Despite this interest, there is remarkably little population-based data available to elucidate the relationships between axis II and axis I disorders. Most studies

to date have been limited to psychiatric inpatients and outpatients (4-8). Because patients may be selected on the basis of degree of emotional distress, health-seeking behavior, and types of psychiatric disorders, a spurious association between personality and other psychiatric disorders cannot be ruled out in studies based on clinical samples (9).

The objective of the present study was to determine if there are specific relationships between axis II and axis I disorders. We restricted our investigation to two *DSM-III* personality disorders—compulsive and antisocial personality disorders—and three *DSM-III* axis I disorders—generalized anxiety disorder, alcohol use disorders (alcohol abuse and alcohol dependence), and simple phobia. Subjects were selected from a survey of household residents and examined by psychiatrists using a semistructured method to diagnose *DSM-III* axis II and axis I disorders.

METHOD

Sampling

A two-stage population survey was conducted at The Johns Hopkins Medical Institutions in 1981 as part of the

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Epidemiological Catchment Area Program of the National Institute of Mental Health (NIMH). The survey population comprised household residents of eastern Baltimore, an area with approximately 175,000 adults living in about 93,000 households. After a probability sampling of households in the area, residents of the selected households who were between the ages of 18 and 64 years were randomly selected for interview. All older residents of these households were also selected (10).

The first stage of the survey involved a screening interview of 3,481 participants that was conducted by specially trained nonphysician surveyors. The interview instrument contained eight distinct screens for evidence of psychopathology, including elements from the NIMH Diagnostic Interview Schedule (11), the General Health Questionnaire (12), and the Mini-Mental State examination (13).

All subjects who were deemed "filter positive" for *DSM-III* psychiatric disorders (i.e., scored positive on one or more of the eight screens), and a 17% random sample from the entire group of 3,481 interviewees, were selected for the second stage of the survey, referred to as the clinical reappraisal. This was a diagnostic reevaluation of subjects who had previously been interviewed. A total of 1,086 subjects were selected for the clinical reappraisal, and 810 (75%) completed the examination. There were no obvious differences in demographic characteristics or scores on screening instruments between respondents and nonrespondents (14).

Clinical Reappraisal Examination

Each subject was examined by one of four board-certified or board-eligible psychiatrists who were graduates of The Johns Hopkins Residency Program. The psychiatrists remained completely blind to all information gathered during the first-stage interview. A comprehensive psychiatric interview employing a semistructured format, the Standardized Psychiatric Examination, was performed. This examination was designed to provide a thorough assessment of the subject's personal history, medical and psychiatric problems, and present mental state, as well as an evaluation of personality.

The Standardized Psychiatric Examination was developed specifically for this study. At the time of its development, no other instrument was available that could be used to record all information required to make most of the *DSM-III* diagnoses. The instrument included all 140 items of the ninth edition of the Present State Examination (15) and supplemented these with other items relevant to *DSM-III* nomenclature. This method emphasized current mental status, although information about past psychiatric history also was obtained. The four psychiatrists held regular conferences and tested themselves by means of videotapes of particular interviews so as to maintain high diagnostic consensus and interrater agreement. The reliability of the Standardized Psychiatric Examination has been described elsewhere (16).

Diagnosis and Scaling of Personality Disorders

When this study was designed in 1980, there were no diagnostic instruments for *DSM-III* personality disorders. We therefore employed an approach that, although not expressly developed for *DSM-III*, could be adapted for that purpose. This approach has been previously described (17).

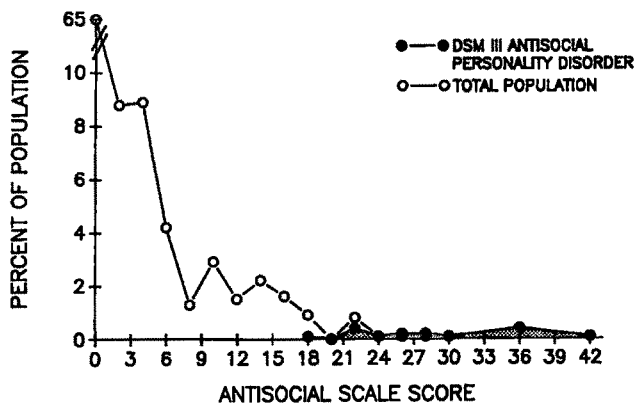
In diagnosing *DSM-III* personality disorders, the examining psychiatrist tried to discern in the subject an enduring pattern of specific behaviors and reactions, as defined in the *DSM-III* manual. For the diagnosis of compulsive personality disorder, the psychiatrist discerned an enduring pattern of specific behaviors characterized by perfectionism, stubbornness, indecision, excessive work devotion, and emotional constriction. For the diagnosis of antisocial personality disorder, the psychiatrist sought an enduring pattern of specific antisocial behaviors, as defined in *DSM-III*.

Two methods were used to delineate traits for compulsive and antisocial personality disorders. In the inventory method, the examining psychiatrist was required to rate abiding characteristics on a 4-point scale ranging from 0 (absent) to 3 ("likely to result in distress under minor life stress") for compulsive personality and a 3-point scale for antisocial personality. These inventory decisions were based on judgments by the psychiatrist of historical information provided by the subject, as well as on the behavior of the subject that emerged spontaneously during the interview. As an integral part of the evaluation, the psychiatrist considered various aspects of the subject's past that illuminated adaptive responses. These aspects included parental relationships, sibling relationships, childhood adjustment and behaviors, schooling, occupational history, legal history, sexual history, marital history, and interests and leisure activities.

The second method required that the examiner ask a series of direct questions about particular traits and thereby reach a confirming or additional opinion on these character features. The scores for each of the five features of compulsivity were then summed in order to arrive at a compulsive personality score, and the scores of the 21 antisocial features were summed to arrive at an antisocial personality score. These scores ranged between 0 and 15 and between 0 and 42, respectively.

Final diagnoses of compulsive and antisocial personality disorders were generated by algorithms based on *DSM-III* criteria. Similarly, diagnoses of generalized anxiety disorder, simple phobia, and alcohol use disorders (alcohol abuse and alcohol dependence) were based on strict *DSM-III* criteria for symptoms and signs evident in the month before the examination. The internal construct validity of the personality disorder scales was evaluated by dichotomizing the ratings for each component trait into "absent" or "present" and computing intertrait tetrachoric correlations with a statistical program, LISCOMP (18). These correlations ranged from 0.33 to 0.68 for the five compulsive items and from 0.23 to 0.87 for the antisocial items. Most correlations were greater than 0.50.

FIGURE 1. Antisocial Personality Disorder Scores in a Community Sample of 810 Subjects, Weighted to the Population of Eastern Baltimore, 1981



Data Analysis

The distributions of personality scores were extrapolated to the general population of eastern Baltimore by weighting the cases according to sampling strata and response rates and adjusting to the 1980 census (10). Logistic regression analysis was employed to evaluate the associations between personality scores and axis I disorders (19). Age, gender, race, and filter status (i.e., whether the subject scored positive on any of the eight screens for psychiatric disorders) were controlled in these analyses. Filter status was controlled to ensure that any observed relationships between axis II and axis I disorders were not biased by the strategy for selecting subjects for the clinical reappraisal sample. The relative odds values obtained from these analyses estimate the increase in odds of the specific axis I disorder for each unit increase in score on the personality scale.

RESULTS

Distribution of Personality Scores

The distribution of compulsive personality scores in the population of eastern Baltimore has been reported previously (17). About 50% of the population had a score of 0 on this scale. Nearly 20% had a score of 1, and the remaining 30% had a score greater than 1. Persons meeting *DSM-III* criteria for the diagnosis of compulsive personality disorder (1.7% of the population) were at the upper extreme of the compulsive personality score distribution, with scores of 8 and above.

Figure 1 shows the distribution of antisocial personality scores in the clinical reappraisal sample, weighted to the population of eastern Baltimore. Nearly 66% of the population had a score of 0 on this scale. Approximately 20% had a score between 1 and 6, and the remaining 14% had a score greater than 6. Persons who met *DSM-III* criteria for the diagnosis of antisocial personality disorder (1.5% of the population) were at the

extreme of the antisocial scale distribution, with scores of 18 and above.

Personality and Axis I Disorders

The prevalence of *DSM-III* generalized anxiety disorder, alcohol use disorders, and simple phobia in subjects, as a function of scores on the compulsive and antisocial personality scales, were investigated. The prevalence of generalized anxiety disorder was strongly related to compulsive personality score; it ranged from 0.7% for those with a score of 0 to over 9% for those with a score of 3 and above (χ^2 for trend=20.5, $df=1$, $p<0.001$). When age, sex, race, and filter status were controlled in a logistic regression model, the odds of having generalized anxiety disorder increased by 50% for every unit increase in compulsive personality score (estimated relative odds=1.54, 95% confidence limits=1.3–1.8, $p<0.001$).

The prevalence of simple phobia also was related to compulsive personality score, ranging from 15% for those with a score of 0 to 27% for those with a score of 3 and above (χ^2 for trend=10.2, $df=1$, $p=0.001$). From logistic regression analysis, the odds of *DSM-III* simple phobia increased with compulsive personality score (relative odds=1.1, 95% confidence limits=1.02–1.2, $p=0.02$).

In contrast, there was an inverse relationship between the prevalence of alcohol use disorders and compulsive personality score (χ^2 for trend=3.3, $df=1$, $p=0.07$). From logistic regression analysis, the odds of alcohol use disorders declined as compulsive personality score increased (estimated relative odds=0.9, 95% confidence limits=0.7–1.1, $p=0.27$).

A different pattern emerged for the relationships between the three *DSM-III* axis I disorders and antisocial personality score. There was no relationship in the prevalence of generalized anxiety disorder as a function of antisocial personality score (χ^2 for trend=0.2, $df=1$, $p=0.66$). From logistic regression analysis, there was an inverse relationship between the odds of generalized anxiety disorder and antisocial personality score that did not reach statistical significance (estimated relative odds=0.9, 95% confidence limits=0.7–1.1, $p=0.24$).

There was no relationship between the prevalence of simple phobia and antisocial personality score (χ^2 for trend=0.01, $df=1$, $p=0.92$). The odds of simple phobia did not change with antisocial personality score (estimated relative odds=1.0, 95% confidence limits=0.98–1.1, $p=0.30$).

In contrast, the prevalence of alcohol use disorders increased in a dose-response fashion with antisocial personality score, ranging from 4% in those with a score of 0 to 22% in those with a score of 3 and above (χ^2 for trend=42.7, $df=1$, $p<0.001$). From logistic regression analysis, the odds of alcohol use disorders increased 10% for each unit increase in antisocial personality score (estimated relative odds=1.1, 95% confidence limits=1.03–1.13, $p<0.001$). These results

did not change appreciably after removal of the alcohol use item from the antisocial personality scale.

Dose-response relationships are illustrated in figure 2, which shows the probabilities, predicted from logistic models, of generalized anxiety disorder as a function of compulsive personality disorder score and of alcohol use disorders as a function of antisocial personality disorder score.

DISCUSSION

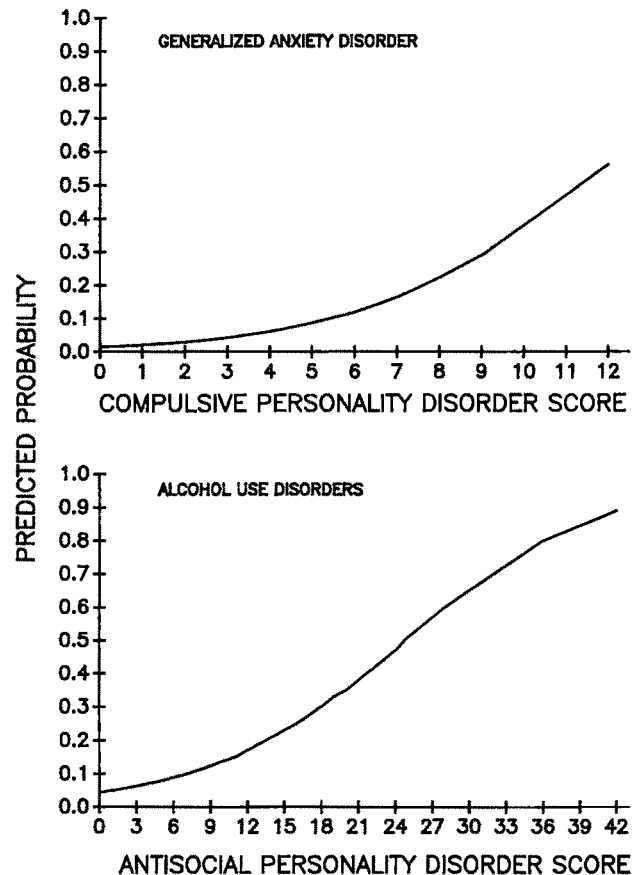
We employed a dimensional perspective to investigate specific relationships between compulsive and antisocial personality features and three axis I disorders in a population-based sample of household residents in eastern Baltimore. Psychiatric diagnoses were made by psychiatrists using a semistructured, standardized instrument. The personality scales were found to have acceptable internal construct validity. The distributions of compulsive and antisocial personality scores in the population demonstrate the arbitrary nature of cutoff values for the definition of *DSM-III* compulsive and antisocial personality disorders and support the use of the dimensional, scaled approach for these personality features.

Controlling for age, sex, race, and filter status in logistic regression models, we found that increasing scores on the compulsive personality scale were associated with a significantly greater odds of generalized anxiety disorder and simple phobia and a smaller odds of alcohol use disorders. In contrast, increasing scores on the antisocial personality scale were associated with a smaller odds of generalized anxiety disorder and a significantly greater odds of alcohol use disorders but showed no relationship with simple phobia. There did not appear to be distinct thresholds for these relationships.

Our findings are generally consistent with clinical studies showing a relationship between compulsive personality and anxiety disorders (20, 21). For example, Alnæs and Torgersen (4) found that simple phobia was more than twice as prevalent in outpatients with compulsive personality disorder as in outpatients with other personality disorders. Gasperini et al. (22) found compulsive personality disorder in 15% of 46 outpatients with generalized anxiety disorder, compared to 4% of nonpatient control subjects (our calculations: $p=0.06$, Fisher's exact test). Our findings are also consistent with clinical and population-based studies showing a strong relationship between antisocial personality and alcohol use disorders (23–25). Our findings of an inverse relationship between compulsive personality and alcohol use disorders and between antisocial personality and generalized anxiety disorder await further investigation in community samples.

Conclusions drawn from this study must be tempered by several methodological limitations. First, additional informants were not available for validating personality attributes reported by the subjects (26). This might be particularly problematic in the case of

FIGURE 2. Predicted Probabilities of Generalized Anxiety Disorder and Alcohol Use Disorders, by Compulsive and Antisocial Personality Disorder Scores in a Community Sample of 810 Subjects in Eastern Baltimore, 1981



ratings of antisocial personality, which relied heavily on subjects' reports of past behaviors. Second, given that assessment of mental status occurred at a single point in time, it may have been difficult to discriminate stable personality features from symptoms (27). However, the examining psychiatrist attempted to elicit enduring personality features over the subject's entire life span. Clarification of the relationships between axis I and axis II disorders will be enhanced by the employment of prospective designs and additional validated scales and dimensions, with assessments of state and trait made by researchers who are blind to each other's assessments (17).

Our finding of specific relationships between dimensionally scaled personality disorders and axis I disorders have important theoretical and clinical implications. These relationships are analogous to those involving intelligence (28). Parallels between this construct and that of personality measured on dimensions can be useful.

Mental retardation is described in terms of categories in *DSM-III* and other nomenclatures. These categories reflect scores on a dimension, intelligence, that is assessed by specific tests. It is found that an individual's probability of developing difficulties correlates nega-

tively with his or her score on a measured intelligence scale. However, the distress of the intellectually limited individual may be evident only under adverse circumstances or in the face of increasing burdens; it is in these situations that his or her vulnerabilities emerge. The actual precipitant for evoking distress is usually specific, i.e., being faced with a situation that taxes problem-solving abilities. Emotional responses may include anxiety, demoralization, and depression.

A variety of personality dimensions have been proposed (29–32). As with intelligence, individuals on the extremes of these dimensions are vulnerable to develop specific problems. For example, in clinical settings, anxiety is common in introverted, quiet, or compulsive individuals, whereas depression is often found in borderline individuals (33). Misbehavior such as alcoholism, drug use, and self-injury occurs more often in extroverted and sociopathic individuals (34).

These mental states or behaviors emerge when the individual is faced with adverse situations or increased burdens. The emotional reactions and behaviors of the individual can be construed as the consequence of a potential defined by aspects of the individual's personality, as well as by provocations exerted by environmental circumstances. This formulation has been described as the "neurotic paradigm" (28).

The adversity may be specific to the vulnerability, such as failure at work for the compulsive individual or inability to fulfill personal goals for the antisocial person. In our view, the threshold for emergence of distress and demoralization in a person confronted with adversity is influenced by the individual's position on the underlying continuum of the personality dimension, as well as by the nature of the specific adversity. This threshold also may be affected by other personal attributes (for example, intelligence, educational attainment, other personality characteristics), the presence of social supports, and previous experience in managing difficult situations.

The nature of personality remains elusive, and ultimate criteria for the validation of personality features await clarification. Nevertheless, as demonstrated in the present investigation, the measurement of personality dimensions has clinical relevance. By helping to identify individuals with specific vulnerabilities, reliable dimensional assessments of personality may point the way toward specific strategies for the treatment and prevention of psychiatric disorders.

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Posttraumatic Adaptation and Distress Among Adult Burn Survivors

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Objective: The purpose of this study was to examine the prevalence, natural history, and psychosocial impact of posttraumatic symptoms in adult burn survivors. **Method:** Forty-three adult inpatients at a regional burn center were assessed at discharge with standardized instruments to determine the presence of psychiatric disorder, assess personality, and quantify depression. Thirty-one patients were evaluated 4 months after discharge. **Results:** Posttraumatic stress disorder was diagnosed in 7% of patients at discharge and in over 22% of patients at follow-up. Symptoms of avoidance and emotional numbing (DSM-III-R criterion C symptoms) tended to emerge after discharge from the hospital. While posttraumatic symptoms were associated with symptoms of depression, they were not strongly associated with psychosocial adjustment to illness; psychosocial adjustment was more strongly related to aspects of personality, the injury itself, and its treatment. **Conclusions:** Since adult burn survivors often develop new symptoms of posttraumatic distress after leaving the hospital, longitudinal surveillance is required to detect new cases and provide appropriate treatment. Survivors at risk for poor psychosocial adjustment after discharge may be identifiable during hospitalization, and preventive treatment strategies should be developed and tested for this population.

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Burn injury—a painful, frightening, and extraordinary trauma—may precipitate posttraumatic symptoms in at least some burn survivors. In a study predating DSM-III, Andreasen and Norris (1) described transient “phobic” and “traumatic” neuroses in many burn survivors. More recently, Courtemanche and Robinow (2) published two illustrative case reports of DSM-III posttraumatic stress disorder (PTSD) in burn victims, and Patterson et al. (3) found that 29% of hospitalized burn survivors met criteria for DSM-III PTSD at some point before discharge.

While these papers illustrate the importance of screening burn patients for posttraumatic distress, they leave unanswered many questions about the prevalence, natural history, and functional implications of

PTSD in this population. One significant unsettled question is the time course of posttraumatic symptoms. Patterson et al. (3) found persistent PTSD (at telephone follow-up 40 days after discharge) in only one of 11 burn survivors who had met criteria for PTSD in the hospital, which suggests that posttraumatic symptoms may be short-lived in this population. However, since Patterson et al. did not perform follow-up interviews of patients who had *not* had PTSD in the hospital, the true prevalence of PTSD at follow-up could not be stated. It is entirely possible that PTSD might have emerged after discharge in patients who had had few, or even *no*, posttraumatic symptoms in the hospital.

Equally uncertain is the relationship between posttraumatic distress and postburn psychosocial adjustment to illness. While it is plausible that PTSD symptoms could hinder postburn psychosocial rehabilitation, this has not been demonstrated among burn patients diagnosed by DSM-III-R criteria, and one study of World War II prisoners of war suggests that even severe symptoms of PTSD are compatible with considerable preservation of psychosocial functioning (4). Furthermore, there is evidence that postburn disability may be related to a variety of clinical variables (e.g., aspects of the burn or its treatment, the patient's personality or premorbid psychopathology) that are independent of the emergence of PTSD symptoms (1, 5).

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The purposes of this study were to describe the prevalence, clinical phenomenology, and clinical correlates of PTSD and its component symptoms among adult burn survivors and to examine the relationship of these symptoms to postburn psychosocial adjustment.

METHOD

Subjects for this study were drawn from the 20-bed inpatient unit of a regional burn center located in an urban medical center. Patients were routinely screened for delirium and other psychiatric disorders soon after admission and followed clinically until discharge. Adult patients who were hospitalized for over 48 hours, who were approaching discharge, and who were not persistently delirious or otherwise inaccessible to interview were invited to participate in the study. Participating subjects took a battery of tests including the Structured Clinical Interview for DSM-III-R (SCID) (6), the Beck Depression Inventory (7), the NEO Personality Inventory (8), and the Millon Clinical Multiaxial Inventory—II (9).

An attempt was made to reinterview the subjects 4 months after discharge. The SCID was readministered over the telephone to subjects who could be reached only in that manner. In addition, a research assistant mailed to all located subjects a packet containing the Beck Depression Inventory and the Psychosocial Adjustment to Illness Survey (10, 11), a standard questionnaire designed to measure post-illness functioning in seven domains: health care orientation, vocational environment, domestic environment, sexual relationships, extended family relationships, social environment, and psychological distress.

Student's *t* test was used to compare group means, and Pearson correlation coefficients were calculated to evaluate the relationships between continuous variables. Relationships between dichotomous variables were evaluated with the chi-square test.

RESULTS

During the study period, 134 adults were admitted to the unit. Of these, 68 could not be given the formal test battery because of death (*N*=14), discharge within 48 hours (*N*=41), persistent delirium (*N*=10), severe attention deficit disorder (*N*=1), or nondelirious psychotic states (*N*=2). Of those able to participate (*N*=66), 43 gave consent and completed the diagnostic interview.

Efforts were made to contact all study patients 4 months after discharge. Twenty-nine (67.4%) were contacted and agreed to retake the SCID; in addition, two patients who had not been tested at discharge entered the study and were given the SCID. Seventeen patients completed and returned the Psychosocial Adjustment to Illness Survey and the Beck Depression Inventory. Those who completed the SCID at follow-up were compared to the 14 who did not; no significant differences were found between these groups in age,

sex, level of education, total body surface area burned, length of stay, or type of burn.

Thirty-five patients (81.4%) in the study were men, and 30 (69.8%) were white. Their average age was 34.7 years (*SD*=11.8). Twelve (27.9%) had a SCID lifetime diagnosis of major depression, while 16 (37.2%) and 10 (23.3%) had lifetime diagnoses of alcohol and marijuana abuse or dependence, respectively. Length of hospital stay averaged 21.6 days (*SD*=21.9). Twelve (27.9%) had burns involving at least 25% of total body surface area, and 23 (53.5%) had facial involvement. Thirty-one (72.1%) had flame or flash burns, while the remaining 12 (27.9%) had chemical, electrical, or scald injuries.

PTSD

At the time of discharge, only three patients (7.1%) met all *DSM-III-R* criteria for PTSD, including the 1-month duration criterion. An additional three patients met all criteria for PTSD *except* for the 1-month duration criterion.

At 4-month follow-up, of the three patients who had met full criteria for PTSD at discharge, one still had PTSD and one was completely symptom free. The other was lost to follow-up. Of the three who had met all criteria except the 1-month duration criterion, one had PTSD at 4 months and one met criteria B (i.e., reexperiencing symptoms) and D (i.e., increased arousal); the other was lost to follow-up. Overall, then, of the four most symptomatic patients who were available for follow-up, three had significant symptoms 4 months after discharge.

Of the 31 patients who took the SCID at 4-month follow-up, seven (22.6%) met full criteria for PTSD. One of these had met full PTSD criteria and one had met all but the 1-month duration criterion at discharge. The remaining five were new cases.

Individual Symptoms of Posttraumatic Distress

Individual symptoms of posttraumatic distress were more common than the fully expressed syndrome of PTSD at discharge and remained common at 4-month follow-up, sometimes emerging in persons who had lacked these symptoms at discharge.

Reexperiencing symptoms. Twenty-five of 43 patients (58.1%) had at least one reexperiencing symptom (i.e., met PTSD criterion B) at discharge (table 1). Of these 25, 19 were available for follow-up at 4 months, and 14 continued to report a reexperiencing symptom at that time.

Of the 31 patients who took the SCID at 4-month follow-up, 19 (61.3%) reported a reexperiencing symptom at that time. In four of these cases, the symptoms had *not* been present at discharge; in one case, the symptomatic status at discharge was not known. Thus, in only four cases were reexperiencing symptoms present at follow-up in patients who had not had such symptoms at hospital discharge.

TABLE 1. Reexperiencing of PTSD Symptoms (DSM-III-R Criterion B) by Adult Burn Survivors at Discharge and 4-Month Follow-Up

PTSD Symptoms	Discharge (N=43)		4-Month Follow-Up (N=31)	
	N	%	N	%
Intrusive memories	16	37.2	14	45.2
Recurrent dreams	11	25.6	10	32.3
Flashbacks	6	14.0	6	19.4
Intense distress at similar events	13	30.2	11	35.5
Any ^a	25	58.1	19	61.3

^aMet criterion B.**TABLE 2. Symptoms of Avoidance and Emotional Numbing (DSM-III-R Criterion C) in Adult Burn Survivors at Discharge and 4-Month Follow-Up**

PTSD Symptoms	Discharge (N=43)		4-Month Follow-Up (N=31)	
	N	%	N	%
Avoidance of thoughts related to event	17	39.5	12	38.7
Avoidance of activities related to event	9	20.9	13	41.9
Inability to recall aspects of event	4	9.3	6	19.4
Diminished interest in usual activities	6	14.0	6	19.4
Feelings of estrangement from others	7	16.3	2	6.5
Restricted range of affect	4	9.3	2	6.5
Sense of foreshortened future	11	25.6	11	35.5
At least three symptoms ^a	8	18.6	8	25.8

^aMet criterion C.

Symptoms of avoidance and emotional numbing. Eight of 43 patients (18.6%) had three or more symptoms of avoidance or emotional numbing (i.e., met PTSD criterion C) at the time of discharge (table 2). Of these eight, five were available for 4-month follow-up, and two of these still met criterion C.

Of the 31 patients who took the SCID at 4-month follow-up, eight (25.8%) met criterion C at that time. Of these eight, six had not met this criterion at discharge. Thus, the majority of patients who reported significant symptoms of avoidance/numbing at 4-month follow-up had developed these symptoms after discharge from the hospital.

Symptoms of increased arousal. Thirteen of 43 patients (30.2%) had at least two symptoms of increased arousal (i.e., met PTSD criterion D) at discharge (table 3). Of these 13, 10 were available for follow-up, and six still met criterion D.

Of the 31 patients who took the SCID at 4-month follow-up, 14 (45.2%) met criterion D at that time. Of these 14, eight had not met this criterion at discharge. Thus, many patients reporting significant symptoms of increased arousal at 4-month follow-up had developed these symptoms after discharge.

TABLE 3. Symptoms of Increased Arousal (DSM-III-R Criterion D) in Adult Burn Survivors at Discharge and 4-Month Follow-Up

PTSD Symptoms	Discharge (N=43)		4-Month Follow-Up (N=31)	
	N	%	N	%
Difficulty sleeping	11	25.6	11	35.5
Increased irritability	8	18.6	9	29.0
Difficulty concentrating	6	14.0	4	12.9
Hypervigilance	8	18.6	13	41.9
Increased startle response	11	25.6	10	32.3
Physiological reactions to event	2	4.7	2	6.5
At least two symptoms ^a	13	30.2	14	45.2

^aMet criterion D.

Posttraumatic Distress and Mood, Burn Type, and Personality

Mood. At discharge, Beck Depression Inventory scores were significantly higher among patients who met criterion C (i.e., avoidance/numbing) (scores of 15.0 versus 7.9; $t=-2.18$, $df=36$, $p=0.04$) and criterion D (i.e., increased arousal) (scores of 14.7 versus 7.0; $t=-3.01$, $df=36$, $p=0.005$) than among other patients. There were no significant relationships between reexperiencing symptoms and Beck Depression Inventory scores.

Patients with PTSD at 4-month follow-up were marginally more depressed than other patients (Beck Depression Inventory scores of 15.0 versus 8.2; $t=-1.72$, $df=13$, $p=0.11$). Two PTSD patients met criteria for major depression and one met criteria for dysthymia at the time of follow-up.

Burn type. Twenty-one (67.7%) of 31 patients suffering flame or flash burns had a reexperiencing (criterion B) symptom at discharge; in contrast, four (33.0%) of 12 patients who had sustained other types of burns (e.g., chemical, electrical) reported such symptoms. This difference was marginally significant ($\chi^2=2.9$, with Yates's correction, $df=1$, $p=0.09$). There were no relationships between type of burn and other posttraumatic symptoms.

Personality. Of the patients who took the NEO Personality Inventory at discharge, those who met criterion B at discharge (N=9) scored lower on the inventory domain of openness than those who did not have such symptoms (N=17) (scores of 46.4 versus 53.0; $t=2.33$, $df=24$, $p=0.03$), and those who met criterion C (i.e., avoidance/numbing) (N=3) scored lower on the inventory domain of extraversion than those who did not (N=23) (scores of 46.7 versus 59.8; $t=3.86$, $df=24$, $p=0.001$). In addition, those who met criterion D (i.e., increased arousal) (N=6) scored higher on the inventory domain of neuroticism than those who did not (N=20) (scores of 58.5 versus 48.5; $t=-2.93$, $df=24$, $p=0.007$).

Of the patients who completed the Millon Clinical Multiaxial Inventory—II at discharge, those who met criterion C (i.e., avoidance/numbing) (N=4) were more schizoid than those who did not (N=30) (scores of 26.5

versus 17.0; $t=-2.85$, $df=32$, $p=0.008$). They were also more avoidant (scores of 35.3 versus 14.6; $t=-3.10$, $df=32$, $p=0.004$), schizotypal (scores of 32.5 versus 14.5; $t=-2.76$, $df=32$, $p=0.01$), and borderline (scores of 38.3 versus 18.5; $t=-2.55$, $df=32$, $p=0.02$). Those who met criterion D (i.e., increased arousal) ($N=10$) scored higher on the borderline scale (scores of 30.8 versus 16.7; $t=-2.58$, $df=32$, $p=0.02$) than those who did not ($N=24$).

Intoxication Upon Admission and Posttraumatic Distress

Blood and urine toxicology screens were ordered at the time of admission for 35 of the 43 patients. Six (17.1%) were positive for alcohol, five (14.3%) for cannabis, three (8.6%) for cocaine, and one (2.9%) for a noncocaine stimulant. Thirteen (37.1%) were negative, and seven (20%) were positive for nicotine, caffeine, and/or therapeutic drugs.

Five (83.3%) of the six patients with detectable blood alcohol levels at admission met criterion D (i.e., increased arousal) at discharge; in contrast, only six (20.7%) of the 29 other patients (including those with detectable levels of other drugs) did so ($\chi^2=6.38$, with Yates's correction, $df=1$, $p=0.01$). Patients with detectable blood alcohol levels were not significantly more likely than other patients to meet criterion B (i.e., reexperiencing symptoms) or C (i.e., avoidance/numbing). There was no relationship between posttraumatic distress and intoxication with any other substance at the time of admission, and there was no relationship between intoxication with any substance, including alcohol, at the time of admission and posttraumatic symptoms at 4-month follow-up.

Other Variables

The likelihood of reporting posttraumatic distress (i.e., meeting criteria B, C, and D or having PTSD) at discharge was not significantly influenced by age, sex, length of hospital stay, total body surface area burned, presence or absence of facial involvement, or the experience of delirium during the hospitalization.

Predictors of Posttraumatic Distress at 4 Months

A number of variables were examined to determine whether clinical features observable at discharge predicted the presence of posttraumatic distress at 4-month follow-up. Patients who had a reexperiencing (criterion B) symptom at follow-up had reported lower openness on the NEO Personality Inventory at discharge (scores of 45.0 versus 51.9; $t=2.27$, $df=19$, $p=0.04$) than other patients. Patients who met criterion C at follow-up had scored lower on the narcissism scale of the Millon inventory—II at discharge (scores of 31.2 versus 40.0; $t=2.06$, $df=25$, $p=0.05$) than other patients. There were no other significant relationships between personality (assessed at discharge) and posttraumatic symptoms reported at 4-month follow-up. There were

also no significant relationships between posttraumatic symptoms at follow-up and other clinical data obtained during the hospitalization, including demographic variables, type of burn, length of stay, presence or absence of delirium, and alcohol intoxication at the time of admission.

Correlates of Postburn Adjustment

There were no significant relationships between postburn adjustment, as measured by the Psychosocial Adjustment to Illness Survey at 4-month follow-up, and the likelihood of having PTSD or of meeting criterion B, C, or D. In contrast, there were significant relationships between scores on the survey at 4-month follow-up and aspects of the injury itself, the treatment provided, and the personality of the victim. The greater the extent of facial involvement, the poorer the adaptation in the survey's social ($r=0.68$, $N=17$, $p<0.01$) and sexual ($r=0.65$, $N=17$, $p<0.01$) domains. Social impairment was also correlated with the extent of sex organ injury ($r=0.67$, $N=17$, $p<0.01$). Those who were delirious during the hospitalization had poorer vocational adjustment (scores of 10.0 versus 3.78; $t=-2.90$, $df=13$, $p=0.01$) and poorer domestic adjustment (scores of 9.2 versus 4.3; $t=-2.16$, $df=13$, $p=0.05$) at follow-up than those who were not delirious. In addition, length of hospital stay was significantly correlated with problems in the vocational ($r=0.73$, $N=17$, $p<0.001$) and domestic ($r=0.67$, $N=17$, $p<0.01$) environments at follow-up.

Patients with Millon Clinical Multiaxial Inventory—II features of the histrionic, antisocial, passive-aggressive, and/or borderline personality types at discharge were particularly likely to show poor adaptation at 4 months. Impairment in domestic adjustment correlated with antisocial ($r=0.71$, $N=14$, $p<0.01$), passive-aggressive ($r=0.64$, $N=14$, $p<0.01$), and borderline ($r=0.74$, $N=14$, $p<0.01$) features. Problems in relationships with extended family members were related to histrionic ($r=0.64$, $N=14$, $p<0.01$), antisocial ($r=0.67$, $N=14$, $p<0.01$), and passive-aggressive ($r=0.68$, $N=14$, $p<0.01$) traits. Global maladjustment (total Psychosocial Adjustment to Illness Survey score) at 4 months was most strongly correlated with Millon Clinical Multiaxial Inventory—II antisocial ($r=0.74$, $N=14$, $p<0.01$) and borderline ($r=0.69$, $N=14$, $p<0.01$) qualities.

There were no significant relationships between dimensions of personality as measured by the NEO Personality Inventory and postburn adjustment as measured by the Psychosocial Adjustment to Illness Survey.

DISCUSSION

To our knowledge, this is the first study to use standardized instruments and *DSM-III-R* criteria in a prospective, longitudinal examination of PTSD and psychosocial adaptation to illness among burn survivors. The main finding was that posttraumatic symptoms

were very common both at discharge and at 4-month follow-up. The full PTSD syndrome tripled in prevalence between the time of discharge and 4-month follow-up, reflecting the delayed emergence of symptoms of avoidance and emotional withdrawal. Impairments in postburn psychosocial adjustment were less strongly related to symptoms of posttraumatic distress than to aspects of the injury itself and the personality of the survivor. As anticipated, substance abuse, especially alcoholism, was highly prevalent in this population (12), and the prevalence of depression was similar to that found among hospitalized patients in general (13).

The differential time course of PTSD symptoms—the tendency for reexperiencing symptoms (criterion B) to be present in the hospital and for symptoms of avoidance and emotional numbing (criterion C) to emerge after discharge—was an unanticipated finding that might be explained by hospitalization itself. Intrusive thoughts and similar symptoms can readily be experienced by hospitalized patients. On the other hand, fulfillment of criterion C requires the manifestation of avoidance behaviors and the experience of altered emotional reactivity to everyday stimuli. Hospitalized patients have limited opportunities to manifest these symptoms and generally must be discharged before they can judge their ability to face stimuli reminiscent of the burn and to resume interpersonal relationships. Thus, the delayed emergence of criterion C symptoms may reflect delayed exposure to opportunities to experience pertinent symptoms.

While some individuals with PTSD undoubtedly suffer severe functional incapacity, the present data show surprisingly little relationship between symptoms of posttraumatic distress and impairments in postburn psychosocial adaptation. While this finding was unexpected, it is consistent with other studies which show that PTSD is compatible with remarkable functional recovery (4). Since the present data did suggest higher levels of depression among patients with PTSD symptoms, it is possible that a study involving more subjects (to minimize the probability of type II error), longer follow-up, and/or the use of other measures of psychosocial adaptation (e.g., return-to-work records) might show stronger links between psychosocial impairment and PTSD symptoms. For now, however, it is accurate to say that symptoms of PTSD may occur in patients who acknowledge little or no psychosocial disability on a self-report instrument.

The best predictors of impaired postburn psychosocial adaptation were aspects of the injury itself, the treatment course, and the personality of the survivor. Burns involving the face and the sexual organs were associated with postburn impairments in the social and/or sexual domains. Patients who were delirious in the hospital and who had longer hospital stays had poorer adjustment in the domestic and vocational domains. Patients with prominent passive-aggressive, antisocial, and borderline personality features had difficulties in

several domains of postburn adjustment, perhaps reflecting long-standing and preexisting difficulties, especially in interpersonal relationships.

These findings have implications for both clinical care and future research. The delayed emergence of posttraumatic symptoms in many patients suggests the need for longitudinal surveillance of all burn survivors to allow for detection of new symptoms and provision of appropriate treatment. The relationships between postburn psychosocial adaptation and aspects of the injury, its treatment, and the personality of the patient suggest the potential for early identification of burn survivors at high risk for poor adjustment and for the development and evaluation of preventive educational and psychotherapeutic (14) treatment strategies for burn survivors with these high-risk characteristics. The absence of strong relationships between posttraumatic symptoms and postburn psychosocial adjustment was surprising and may have resulted, at least in part, from the small size of the follow-up cohort. To further clarify the functional implications of posttraumatic symptoms in this population, longitudinal studies involving larger numbers of subjects and longer follow-up intervals should be undertaken.

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Pubertal Stage and Panic Attack History in Sixth- and Seventh-Grade Girls

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Objective: Although the incidence of first panic attacks appears to peak during adolescence, little is known about which features of adolescence contribute to the risk of a first panic episode. The purpose of this study was to compare the relative importance of age and pubertal stage in explaining the occurrence of panic attacks in adolescents. **Method:** From a school-based sample of sixth- and seventh-grade girls, 754 subjects completed both a structured clinical interview determining history of one or more panic episodes and a self-assessment of Tanner stages of pubertal development. A multiple logistic regression analysis was performed with panic attack history as the dependent variable and pubertal stage, age, and their interaction as the independent variables. **Results:** A history of one or more four-symptom panic attacks was found in 5.3% of the girls (N=40). After age was controlled for, pubertal stage was significantly related to panic attack history. At each age, higher rates of panic attacks were found in the more physically mature girls. **Conclusions:** Pubertal stage, after adjustment for the effects of age, appears to predict panic attack occurrence in young adolescent girls. Understanding the link between puberty and panic may offer clues regarding the onset and etiology of panic attacks.

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Early identification of panic disorder is important because of the associated risk for developing agoraphobia and depression (1, 2) and because of the association between panic disorder and mortality from suicide (3) and possibly cardiovascular disease (4, 5). Early onset of an anxiety disorder may also increase the risk for drug abuse in young adults (6). There are effective treatments for panic symptoms, raising the possibility that panic-related morbidity is preventable. The first symptom of panic disorder is the initial panic attack. Not every person who experiences a panic attack will

develop panic disorder. Approximately 10% of the adults in the Epidemiologic Catchment Area (ECA) study reported ever having had a panic attack, whereas the lifetime prevalence for panic disorder in the same study was 1.6% (7). Recognizing risk periods for the beginning stages of panic disorder would facilitate primary and secondary prevention efforts.

Both panic attacks and panic disorder are thought to be uncommon in children (8, 9). There are case reports of panic disorder in children (10-14), but a population-based survey of 792 children 11 years old detected no cases of panic disorder (15). Adolescence, on the other hand, appears to be a period of increased reports of panic symptoms. In the ECA study, for adults with simple panic attacks the peak age at onset was during adolescence (16). In case series from child and adolescent psychiatry clinics (17-21), most patients seen for panic symptoms are adolescents. Although epidemiologic studies indicate that panic disorder is still uncommon during adolescence (22), less frequent panic attacks may not be. In a small pilot study (23), we previously reported a lifetime prevalence of isolated four-symptom panic attacks of 11.6% among 95 ninth-grade students. There may be an increase in the frequency of panic attacks between childhood and adolescence that, to date, has received little systematic evaluation or explanation.

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This possibility that panic symptoms may be more common in adolescents than in children focused our attention on adolescence as a risk period for the occurrence of panic attacks. We wondered whether puberty represents a specific risk factor separate from that of age. While puberty and the associated hormonal changes have been linked to the onset of various psychological symptoms (24), to our knowledge a specific association with panic attacks has not been reported in any population-based study of adolescents, nor do we know of any report of the relative influence of age and puberty. Thus, the purpose of this study was to fill this gap in knowledge by investigating the relationship of pubertal level versus age to history of panic attacks in a representative sample of adolescent girls at various stages of sexual maturation.

METHOD

Subjects

The subject group in this study was a school-based sample of peripubertal girls who were participating in a health curriculum intervention study (J.D. Killen et al., unpublished manuscript). All sixth- and seventh-grade girls enrolled in four middle schools located in two school districts in northern California were eligible to participate in this study. The parents of 19 subjects requested that their children not be involved in the study, leaving 939 eligible to participate. The age range of these students was 10.3–15.6 years. The school districts serve a suburban, ethnically diverse population near a large metropolitan area. This study was undertaken with the approval of our institution's committee for protection of human subjects and involved a passive consent process that afforded the student the opportunity to decline to participate. To maintain confidentiality, each student was assigned an identification number that was used to track all data collected. All assessments were performed at the schools during class periods on 5 consecutive school days.

The general subject variables collected by questionnaire included age, birth date, current grade, and ethnicity.

Structured Interviews

Previous population-based research concerning panic attacks in adolescents (25, 26) has used questionnaires to determine panic attack status. Although sensitive, questionnaires for panic attacks may lack specificity, yielding high false positive rates (27). To avoid this possibility, we determined the history of panic attacks with a structured diagnostic interview similar to that used in our previous work (23).

The Structured Clinical Interview for DSM-III-R—Nonpatient Version (SCID-NP) (28) was used to diagnose panic attacks. Although this instrument has not been standardized in this age group, our previous expe-

rience of using the SCID with adolescents led us to believe that the subjects would comprehend the questions and participate in the interview. Panic attacks attributable to social or simple phobic stimuli were not coded as panic attacks. Medical conditions and stimulants known to precipitate panic attacks were not assessed.

The interviews were performed by 10 trained graduate students in psychology. The training consisted of two 4-hour training sessions, during which the criteria for panic attacks were reviewed and videotaped SCID interviews of patients with panic disorder were observed. The subjects were interviewed in private settings during class periods and were informed that all information was confidential. The two circumstances under which breach of confidentiality was allowed were suicide risk and child abuse. Confidentiality was broken during the structured interview in two cases of suicidality. These cases were uncovered incidentally, as we did not formally ask about suicidal thoughts or intentions.

For estimation of interrater reliability, two interviewers were present during 40 of the interviews. One interviewer performed the interview, and both interviewers rated the subject independently. The kappa coefficients for the interview questions ranged from 0.66 to 1.00. The kappa coefficient for the designation of panic attack versus no panic attack was 0.79. We also compared the proportions of students identified by the 10 interviewers as having had a panic attack, and there was no statistical difference between the proportions.

Tanner Staging

Pubertal development was assessed by self-staging with the method of Duke et al. (29). The students were presented with standardized line drawings and written descriptions of the five stages of breast development and the five stages of pubic hair development (30). The subjects were instructed to select the drawings that best reflected their pubertal levels. While self-rating is not as accurate as physician-determined Tanner stage, previous research in which self-ratings were independently verified by pediatricians indicates that adolescent self-ratings correlate highly with physician-determined stage of pubertal development. For example, in one study of 43 girls aged 9 to 17 (29), self-ratings based on photographs agreed with pediatrician examination ratings in 37 of the 43 cases ($\kappa=0.81$) for breast stage and in 40 of the 43 cases ($\kappa=0.91$) for pubic hair stage. In a study of 66 girls aged 7 to 12 years (30), self-ratings based on drawings were compared with pediatrician examinations, and the kappa for the older girls, who would be closer in age to the girls in the present study, was 0.73. These findings indicate that girls in this age group can accurately self-assess Tanner stage.

Since Tanner breast stage and Tanner pubic stage were highly correlated in this sample ($r_s=0.66$, $p\leq 0.0001$), Tanner stages are reported as a summary measure to avoid collinearity in regression analyses. The Sexual Maturity Index was used as the summary measure of

Tanner stages (31). The Sexual Maturity Index is the mean (rounded up to the next integer) of the two Tanner stages, breast and pubic hair.

Statistical Analysis

The data were analyzed by using the Statistical Analysis System for the personal computer (32). Two-tailed statistical tests were used to compare groups. Each subject was assigned to one of two groups: 1) those who had experienced at least one four-symptom panic attack in their lifetimes and 2) those not reporting a four-symptom panic attack. Group differences in age were compared by using the Student's *t* test. Ethnic groups were collapsed to include only the ethnic groups that constituted at least 10% of the sample, and the remaining groups were included in the designation of "other." Group differences in ethnicity were compared with a chi-square test statistic.

Multiple logistic regression analysis was performed with panic history as the dependent variable and age, Sexual Maturity Index, and the interaction of age and Sexual Maturity Index as the independent variables. A 5% two-tailed level of significance was used. For significant effects, the adjusted odds ratios with 95% confidence intervals are presented.

RESULTS

Of the 939 eligible subjects, complete interview data were obtained for 823 subjects (87.6%). The 116 for whom we did not obtain complete interview data were absent during the days the assessments were conducted, were present during the days in which the interviews were performed but were not interviewed owing to time constraints involved with conducting interviews during class periods, or did not finish the panic section of the interview. There were no significant differences in age and ethnicity between those completing the interview and the remainder of the sample.

Of the 823 subjects with complete interview data, 754 (91.6%) completed the Tanner staging evaluation. Those who did not complete the Tanner self-rating were either absent on the day it was performed or were unable to comprehend the instructions. There were significant differences in mean age and ethnicity between the 754 subjects who completed the Tanner self-staging and the remainder of the sample. The noncompleters were older, and more of them were Hispanic.

Of the 754 subjects who completed both the interview and the Tanner self-staging, 40 subjects (5.3%) reported having experienced at least one four-symptom panic attack in their lifetimes. An additional four subjects (0.5%) reported having at least one limited-symptom panic attack. There were no significant differences in mean age or ethnicity between those with and those without panic attack histories. Their mean ages were 12.3 (SD=0.8) and 12.4 (SD=0.7) years, respectively. The ethnic distribution of the subjects with

TABLE 1. Multiple Logistic Regression Analysis of Relationship of Panic Attack History to Sexual Maturity and Age in 754 Sixth- and Seventh-Grade Girls

Variable	Parameter Estimate	SE	χ^2 (df=1)	p
Sexual Maturity Index ^a	0.8	0.2	12.2	0.0005
Age	-0.5	0.3	3.0	0.09
Interaction	0.2	0.3	0.8	0.38

^aOdds ratio=2.3, 95% confidence interval=1.4-3.6.

panic attacks was as follows: white, 37.5%; Hispanic, 37.5%; Asian, 12.5%; and other, 12.5%. The ethnic distribution of the subjects without panic attacks was white, 44.3%; Hispanic, 22.0%; Asian, 19.3%; and other, 14.4%.

The results of the multiple logistic regression analysis are presented in table 1. The adjusted odds ratio for the association between the Sexual Maturity Index and panic attack history was 2.3 (95% confidence interval=1.4-3.6); i.e., at each age a single point increase in the Sexual Maturity Index was associated with a more than twofold increase in the odds of having had a panic attack. There was no statistically significant effect of age or the interaction between age and the Sexual Maturity Index.

A striking result was the higher prevalence of panic attack history in girls at more advanced stages of pubertal development at any given age (see table 2). Of the 94 girls with a Sexual Maturity Index of 1 or 2, none reported having had a panic attack. Of the 100 girls who had completed puberty, represented by a Sexual Maturity Index of 5, 8.0% reported panic attacks. The increase in reported panic attacks with increasing sexual maturity was not accounted for by increasing age. At any age between 11 and 13, a history of panic attacks was more common in the more sexually mature girls.

DISCUSSION

It is important to note that although this study indicates an association between panic attack history and pubertal stage, it does not provide historical information concerning the exact point, during puberty or before puberty, at which any given subject experienced her first panic attack. Other limitations of this study include the cross-sectional design, the constricted age range of the sample, and the absence of boys. Boys' sexual development at any given age would not be comparable to that for the girls in this study, and we have no information about whether panic and puberty are related in boys. In addition, there was an ascertainment bias in that the subjects who completed both the interview and self-determined Tanner staging were different from the subjects who completed one or neither of the assessments. The noncompleters were significantly older and more commonly Hispanic than were the completers. Since noncompletion was due to ab-

TABLE 2. Prevalence of Panic Attack History According to Age and Sexual Maturity in 754 Sixth- and Seventh-Grade Girls

Sexual Maturity Index ^a	Age ≤11 Years			Age=12 Years			Age ≥13 Years			Total		
	N	History of Panic Attacks		N	History of Panic Attacks		N	History of Panic Attacks		N	History of Panic Attacks	
		N	%		N	%		N	%		N	%
1 or 2	62	0	0.0	31	0	0.0	1	0	0.0	94	0	0.0
3	117	6	5.1	93	1	1.1	21	1	4.8	231	8	3.5
4	84	9	10.7	155	12	7.7	90	3	3.3	329	24	7.3
5	9	0	0.0	38	3	7.9	53	5	9.4	100	8	8.0
Total	272	15	5.5	317	16	5.0	165	9	5.5	754	40	5.3

^aSummary of self-assessed Tanner pubic hair and breast stages; 1=earliest stage, 5=most advanced.

sences and language barriers, the ascertainment bias may reflect attendance patterns and language-related bias rather than avoidance of study participation. Nevertheless, this ascertainment bias may render the findings less generalizable.

It is also important to realize that isolated panic attacks are not necessarily clinically significant. Which and how many of the girls in this study who have experienced one or more panic attacks will go on to develop panic disorder is unknown. Although girls who have had one or more panic attacks may be a high-risk population, longitudinal studies are required to elucidate the natural history of those who experience isolated panic attacks.

It is tempting to speculate that the increasing levels of sex hormones during puberty contribute to the increased occurrence of panic in the later stages of puberty. This study provides no empirical basis for supporting a hormonal explanation over a psychosocial hypothesis. The interaction of hormonal and psychological changes may be most important. Other possible explanations related to puberty include exposure to illicit drugs, separation fears, increased social anxiety, increased sexual activity, or the recently suggested possibility that the neurodevelopment of the noradrenergic system is related to the onset of panic (33).

An important developmental change that occurs during puberty is the emergence of the capacity for abstraction. Nelles and Barlow (8) have argued that the rarity of panic in childhood is related to stages of cognitive development. They contend that children may be incapable of making the necessary false connections between bodily sensations and catastrophic outcomes, which characterize panic sufferers. For example, believing that heart palpitations represent an impending heart attack may require formal operational thought in the Piagetian definition, which children have yet to acquire. On the other hand, evidence from case reports indicates that children do experience panic attacks which are phenomenologically similar to adults' panic episodes (13, 14, 21, 23) and that they respond to similar treatments (19, 21, 34).

Adolescence is a period of high risk for onset of many forms of psychopathology. For example, the incidences of obsessive-compulsive disorder (35), depression in

girls (36), anorexia nervosa (37), and suicide (38) rise abruptly during adolescence. Nevertheless, there remains a paucity of data regarding the role of puberty in the onset of these conditions. The results of this study suggest that assessing pubertal level should become standard in psychiatric risk assessment studies of young adolescents. In addition, efforts aimed at the prevention of morbidity related to panic might best be directed at peripubertal adolescents. More generally, this study reminds us that, although for most adolescents puberty signals the normal transition from childhood to adulthood, for others puberty may herald the beginning of adult forms of psychopathology.

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Tics and Tourette's Disorder: A 2- to 7-Year Follow-Up of 54 Obsessive-Compulsive Children

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Objective: This study examined a hypothesized etiologic relationship between Tourette's disorder and obsessive-compulsive disorder. **Method:** Fifty-four children who had initially participated in treatment protocols for obsessive-compulsive disorder (Tourette's disorder was an exclusionary criterion) were reevaluated 2–7 years later with a neurological examination and a structured interview to establish the presence or absence of tics and Tourette's disorder. The children's first-degree relatives (N=171) were also screened for tic disorders. **Results:** At baseline, 57% (N=31) of the patients had lifetime histories of tics. At follow-up, 59% (N=32) had lifetime histories of tics; eight of these (all males) met the criteria for Tourette's disorder (six had developed the disorder, and two, it could be argued in retrospect, might have met the criteria at baseline). The patients with lifetime histories of tics had greater anxiety, a higher ratio of CSF 5-hydroxyindoleacetic acid to homovanillic acid, and a younger age at onset of obsessive-compulsive disorder than those without tics. The patients with Tourette's disorder differed from other male patients only in having an earlier age at onset of obsessive-compulsive disorder. Of the first-degree relatives, 1.8% (N=3) had Tourette's disorder, and 14% (N=24) had a tic disorder. **Conclusions:** Except for their earlier age at onset of obsessive-compulsive disorder, the patients with Tourette's disorder were indistinguishable from those without. The apparent high rate of tics and Tourette's disorder in the subjects and their relatives is consistent with the hypothesis that in some cases, obsessive-compulsive disorder and Tourette's disorder may be alternative manifestations of the same underlying illness.

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Obsessive-compulsive disorder has been reported in association with a number of basal ganglia disorders, specifically, Sydenham's chorea (1), post-encephalitic Parkinson's disease (2), Huntington's chorea (S. Folstein, personal communication), and Tourette's disorder (3). Of these, obsessive-compulsive disorder has been noted most often in Tourette's disorder; the more recent systematic studies have reported that one-third to one-half of adult (3–5) and child (6) patients with Tourette's disorder are afflicted. Studies of patients with obsessive-compulsive disorder also suggest a relationship between Tourette's disorder and obsessive-compulsive disorder; an

increased prevalence of chronic tics has been noted by several observers (5, 7, 8).

Other compelling evidence for a relationship between Tourette's disorder and obsessive-compulsive disorder comes from family studies of probands with Tourette's disorder (3, 5, 9, 10). Pauls et al. (3) reported that the rate of obsessive-compulsive disorder among 45 first-degree biologic relatives of 13 probands with Tourette's disorder without obsessive-compulsive disorder was 26%. This was higher than the expected rate in the general population and was similar to the rate for relatives of probands who had Tourette's disorder with obsessive-compulsive disorder. The mode of transmission of Tourette's disorder and chronic tics is consistent with autosomal dominant inheritance with incomplete penetrance and sex-influenced expressivity (10). Pauls et al. (3, 10) hypothesized that at least some forms of obsessive-compulsive disorder are etiologically related to Tourette's disorder and chronic tics and that obsessive-compulsive disorder may be an alternative phenotypic manifestation of the gene(s) responsible for Tourette's disorder. At present, however, the exact relationship between Tourette's disorder and obsessive-compulsive

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disorder is unknown, and there are no systematic studies of Tourette's disorder in family members of probands with obsessive-compulsive disorder.

The actual prevalences of Tourette's disorder and chronic tics are unknown, as no large general population samples have been systematically screened for tics. The prevalence of Tourette's disorder in selected populations has been estimated to be 2.9 (11), 5.2 (12), and 40 (13) per 10,000, but the studies have been limited by their sampling techniques. Tic disorders are more common than Tourette's disorder in the general population, and estimates have ranged from 4% to 6% (14-16) to 12% (17, 18). Sampling techniques and varied diagnostic criteria for tics limited these studies, and in several samples nonspecific nervous or unusual movements were included, which may have inflated the estimates.

This report concerns tics and Tourette's disorder at 2- to 7-year follow-up in 54 children and adolescents with severe primary obsessive-compulsive disorder for whom a diagnosis of Tourette's disorder, but not chronic tics, had initially been ruled out. We hypothesized that despite the initial exclusion of Tourette's disorder, some of the patients with obsessive-compulsive disorder would "develop" Tourette's disorder, given the reported association between the two disorders, the presence of tics at baseline among many patients, and the hypothesis that within families of probands with Tourette's disorder the two disorders are etiologically related. The study addressed the following questions. 1) What are the lifetime and current rates of Tourette's disorder and tics at follow-up in child probands with obsessive-compulsive disorder and their first-degree relatives? 2) Is there a characteristic demographic, clinical, laboratory, or familial pattern among probands with obsessive-compulsive disorder and Tourette's disorder or chronic tics that might elucidate a relationship between the conditions?

METHOD

Fifty-four children and adolescents with severe primary obsessive-compulsive disorder who had been consecutively admitted to clomipramine treatment trials conducted between 1985 and 1988 (19, 20) were contacted for follow-up evaluation. At baseline, these 36 boys and 18 girls had a mean age of 13.6 years ($SD=2.0$, range=7-19) and a mean age at onset of obsessive-compulsive disorder of 9.9 years ($SD=3.3$, range=2-16). A diagnosis of Tourette's disorder was an exclusionary criterion for these studies, but a chronic vocal or motor tic was not.

At follow-up, the 54 subjects with obsessive-compulsive disorder had a mean age of 17.4 years ($SD=3.0$, range=10-24). They were reevaluated 2-7 years (mean=3.4 years, $SD=1.0$) after baseline. Information was obtained for all 54 subjects, and 48 (89%) of the patients were seen in person. Information on the remaining six (11%) was available from at least two of the following sources: telephone interview with the patient ($N=3$),

family report ($N=6$), current private physician's report ($N=2$), and medical records ($N=3$).

At baseline evaluation, assessment of lifetime and current *DSM-III-R* tic diagnoses consisted of clinical interviews and administration of the Diagnostic Interview for Children and Adolescents (21) (including the tic section of the parent interview) to a parent and child, review of available medical records, and a neurological examination. Demographic measures, associated comorbidity, and scores on severity rating scales, including the National Institute of Mental Health (NIMH) global scales for obsessive-compulsive disorder, anxiety, depression, and functioning (22), have been reported by Leonard et al. (20). Interrater reliability (κ) between the two raters (H.L.L. and S.E.S.) ranged from 0.91 to 0.97 and is detailed elsewhere (23). Forty-three (80%) of the patients underwent lumbar puncture (24).

At follow-up, the measures were repeated, and the NIMH global obsessive-compulsive disorder score (22) was used as the follow-up rating of the severity of that disorder. Additionally, the Tourette syndrome/tics section-modified of the Yale Schedule for Tourette and Other Behavioral Syndromes (25) was administered to either the parent (about the proband) or the proband, and the Children's Global Assessment Scale (26) was completed. Twenty-two patients had a repeat lumbar puncture; however, those results have not yet been analyzed.

With the use of the Diagnostic Interview for Children and Adolescents (21) or the Schedule for Affective Disorders and Schizophrenia (SADS) (27) (according to the age of the person being interviewed), 170 of the probands' 173 first-degree relatives over 6 years of age were interviewed in person when the probands entered the study. In addition, a forensic psychiatric evaluation of one father was available. Thus, diagnoses were made for 52 mothers (mean age=44.7 years, $SD=4.2$), 51 fathers (mean age=47.6 years, $SD=5.3$), 30 sisters (mean age=17.2 years, $SD=4.6$), and 38 brothers (mean age=15.9 years, $SD=5.4$). (Because two sets of brothers were included among the 54 subjects, for the family data one brother was randomly assigned as the proband and one as the sibling for each family. Thus, 52 probands are referred to for the family data. It should be noted that none of the four brothers had a tic disorder.) Lenane et al. (28) previously reported that among the first-degree relatives of 46 of these 54 probands, 15 parents (17%) and three siblings (5%; age corrected, 35%) had lifetime histories of obsessive-compulsive disorder at baseline. Three additional cases were diagnosed subsequently, at the time of this follow-up. (Two fathers had not acknowledged obsessive-compulsive symptoms at the first evaluation, and one sibling developed them in the interim.) All relatives had been observed for tics and had been asked during the baseline clinical interview about the presence of motor and vocal tics; however, no formal neurological examinations or structured ratings of tics were obtained, other than the Diagnostic Interview for Children and Adolescents—

TABLE 1. Baseline and 2- to 7-Year Follow-Up Data on 54 Male and Female Patients With Obsessive-Compulsive Disorder With and Without a Lifetime History of Tics at Follow-Up

Item	Patients With Lifetime History of Tics (N=32)		Patients Without Lifetime History of Tics (N=22)	
	Mean	SD	Mean	SD
Age at onset of obsessive-compulsive disorder (years) ^a	9.2	3.3	10.8	3.1
Age at follow-up (years)	17.5	3.3	17.4	2.4
IQ	109.7	14.7	104.8	9.4
Baseline CSF measure ^b				
5-HIAA level (age corrected; pmol/ml)	117.2	35.8	108.1	26.4
HVA level (age corrected; pmol/ml)	268.2	93.9	273.3	66.6
5-HIAA/HVA ratio ^c	0.45	0.11	0.40	0.05
MHPG level (pmol/ml)	48.8	11.5	42.0	10.4
Baseline serotonin level (ng/10 ⁸ platelets)	55.5	26.1	50.0	17.6
NIMH global scale rating at baseline				
Obsessive-compulsive disorder	8.5	1.4	8.6	1.4
Depression	4.7	2.1	4.4	2.1
Anxiety ^c	6.5	2.1	4.9	1.7
Functioning	7.6	1.7	7.5	2.1
Response to clomipramine at 5 weeks (%)	27	21	27	28
NIMH global obsessive-compulsive disorder rating at follow-up	5.7	2.9	4.1	2.3
Children's Global Assessment Scale score at follow-up	61.9	20.8	73.7	19.4

^aFrom discriminant analysis, partial $R^2=0.08$, $p<0.05$.^bN=22 for patients with lifetime history of tics; N=21 for patients without lifetime history of tics.^cFrom discriminant analysis, partial $R^2=0.15$, $p<0.05$.

Parent Version (21) for the siblings. At follow-up, the Yale Schedule for Tourette and Other Behavioral Syndromes (Tourette syndrome/tics section-modified) (25) was administered to at least one parent of every family, who reported on all family members, in order to confirm the original tic status and to assess any changes. Forty-eight mothers, 12 fathers, four siblings, and 28 probands were reinterviewed directly about family members, and 27 families had more than one family member interviewed.

BMDP stepwise discriminant analyses with jackknife validation (29) were used to determine which baseline and follow-up variables best discriminated 1) between patients with and without tics and 2) among males with Tourette's disorder, chronic/transient tics, and no tics. This procedure controlled for an otherwise inflated error rate that would have occurred with the use of a large number of univariate tests. Comparisons of specific obsessive-compulsive disorder symptoms between patients with and without tics were made with chi-square tests.

Since not all first-degree relatives had passed through the risk period for developing illness, the rates of tics and obsessive-compulsive disorder were age corrected using known cumulative data on age at onset (30, 31).

We used a modified Stromberg method (32) to correct for each person's age according to the percentage of the risk period for each disorder through which he or she had passed. Statistical comparisons of age-corrected rates of illness between different groups were made with chi-square and Fisher's exact tests. The age of 15 years was arbitrarily assigned to adults who recalled an onset of tics in adolescence but could not be more specific (N=11).

Life table survival analyses that used BMDP program P1L were performed to compute the cumulative hazard function (probability of developing an illness by a certain age) for tics and obsessive-compulsive disorder in the first-degree relatives (29, 33, 34). This procedure yields more information than simple lifetime prevalence estimates, as it allows for the estimation of the risk of an illness at a given age within a given population. To assess the relative effects of several variables simultaneously on the relatives' survival function (not developing illness), the Cox proportional hazards model was used with BMDP program P2L (29, 34). Comparisons between male and female relatives on this hazard function could then be made using the Mantel-Cox statistic (33-35).

RESULTS

The Patients

At baseline, 16 (30%) of the 54 patients with obsessive-compulsive disorder had a current transient or chronic tic, and 31 (57%) had lifetime histories of tics (including the current status). At follow-up, 22 subjects (12 male and 10 female) had no lifetime history of tics, and 32 subjects (24 male and eight female) (59%) had lifetime histories of transient/chronic tics or Tourette's disorder; 17 (31%) had current diagnoses of tics. Of the 32 with lifetime tic diagnoses, eight (15% of the total of 54 patients) met lifetime diagnostic criteria for Tourette's disorder, 12 (22% of the 54) for chronic tics, and 12 for transient tics. At follow-up, from rereview of initial medical records and from additional information obtained from structured interview, it could be argued that two of the eight subjects with Tourette's disorder (all male) might have met the diagnostic criteria for Tourette's disorder at baseline. Thus, six (11%) of 54 subjects who did not meet criteria for Tourette's disorder at baseline "developed" Tourette's disorder in the interim.

Of the 32 patients with lifetime histories of tics, at baseline 17 (53%) also had lifetime histories of an anxiety disorder, seven (22%) had attention deficit hyperactivity disorder, and seven had oppositional/conduct disorder. Of the 22 patients without a lifetime history of tics, 10 (45%) had an anxiety disorder, five (23%) had attention deficit hyperactivity disorder, and four (18%) had oppositional/conduct disorder at baseline.

Among the 32 patients with lifetime histories of tics, nine (28%) had relatives with obsessive-compulsive

TABLE 2. Lifetime Histories of Obsessive-Compulsive Disorder and Tic Disorder Among First-Degree Relatives of 52 Probands With Obsessive-Compulsive Disorder

Measure	Relatives of 34 Male Probands						Relatives of 18 Female Probands						Relatives of All 52 Probands					
	Male (N=62)		Female (N=52)		Total (N=114)		Male (N=27)		Female (N=30)		Total (N=57)		Male (N=89)		Female (N=82)		Total (N=171)	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Tics	17	27 ^a	2	4	19	17	4	15	1	3	5	9	21	24 ^a	3	4	24	14
Age corrected		28		4		17		15		3		9		24		4		14
Obsessive-compulsive disorder	11	18	5	10	16	14	5	19	1	3	6	11	16	18 ^b	6	7	22	13
Age corrected		25		12		19		23		4		13		23		10		17
Total relatives affected	22	35 ^c	6	12	28	25	7	26	2	7	9	16	29	33 ^a	8	10	37	22
Age corrected		35		12		25		26		7		16		33		10		22

^aRate of illness significantly greater in male relatives than in female relatives ($p < 0.005$, Fisher's exact test).

^bRate of illness significantly greater in male relatives than in female relatives ($p < 0.05$, Fisher's exact test).

^cRate of illness significantly greater in male relatives than in female relatives ($p < 0.01$, Fisher's exact test).

disorder, and 13 (41%) had relatives with tics. Among the 22 patients with no lifetime history of tics, seven (32%) had relatives with obsessive-compulsive disorder, and 11 (50%) had relatives with tics.

The sex of the subject, a family history of obsessive-compulsive disorder, a family history of tics, and all variables shown in table 1 were entered into the discriminant analysis. The statistically significant variables best able to distinguish the 32 patients with lifetime histories of tics from the 22 without were, in order of significance, a higher score (more symptoms) on the NIMH global anxiety scale at baseline, a greater baseline ratio of CSF 5-hydroxyindoleacetic acid (5-HIAA) to homovanillic acid (HVA), and a younger age at onset of obsessive-compulsive disorder. Together, these three variables correctly classified 81% of the patients with tics and 57% of the patients without tics, for an overall ability of 69%. There was no difference (by chi-square test) between the presenting major obsessive-compulsive symptoms of patients with and patients without lifetime histories of tics. Washing compulsions were the most frequently reported for both groups, followed by checking and repeating.

At follow-up, although all of the eight patients with Tourette's disorder met the *DSM-III-R* diagnostic criteria, the symptoms were mild. Only four patients were aware that they had a tic disorder, and only two had had a previous medication trial for the tics. All but one of the Tourette's disorder patients had lifetime histories of tics at baseline. Three had attention deficit hyperactivity disorder, one had learning disabilities (visual perceptual), and one had oppositional and conduct disorder. Three patients with Tourette's disorder had a first-degree relative with obsessive-compulsive disorder, and four had a family history of tics (one relative met criteria for Tourette's disorder). The primary presenting symptoms were typical for obsessive-compulsive disorder—specifically, washing rituals (N=5), hoarding (N=1), repeating (N=1), and scrupulosity (N=1).

To see whether the patients with Tourette's disorder differed on any measure (in the previous discriminant analysis) from those with chronic/transient tics and

from those without any tic diagnosis, a second discriminant analysis was performed. Only males were chosen for these comparisons in order to control for any confounding influence of gender. Only a younger age at onset of obsessive-compulsive disorder distinguished the group of patients with Tourette's disorder from the other two groups. Age at onset of obsessive-compulsive disorder distinguished 50% of the patients with Tourette's disorder, 80% of those with tics, and 0% of the patients without tics, for an overall rate of 46%. The mean ages at onset of obsessive-compulsive disorder for the eight boys with Tourette's disorder, the chronic/transient tic group, and the group without tics were 6.5 years (SD=3.5), 10.4 years (SD=2.9), and 11.3 years (SD=3.1), respectively. No significant differences between the three groups were found for the CSF measures: 5-HIAA/HVA ratios for the Tourette's disorder group, the transient/chronic tic group, and the group without tics were, respectively, 0.53 (SD=0.12) (N=3), 0.45 (SD=0.12) (N=11), and 0.40 (SD=0.05) (N=12).

The Families

At follow-up, three (1.8%) of the first-degree relatives (one father and two male siblings) met criteria for a lifetime diagnosis of Tourette's disorder. All three were evaluated in person to confirm the diagnosis. The three different probands whose family members had Tourette's disorder were in three separate patient diagnostic subgroups: obsessive-compulsive disorder and Tourette's disorder, obsessive-compulsive disorder with chronic tics, and obsessive-compulsive disorder without tics.

The age-corrected lifetime prevalence rates of obsessive-compulsive disorder and tic disorders (including chronic, transient, and Tourette's disorder) among the 171 first-degree relatives are presented in table 2. The most striking findings were the apparent high rates of tics (14%) and obsessive-compulsive disorder (17%) among the first-degree relatives of the probands and the fact that illness in relatives was unrelated to the sex of the probands. There were significantly more male rela-

TABLE 3. Lifetime Prevalence of Obsessive-Compulsive Disorder, Tics, and Tourette's Disorder in 171 First-Degree Relatives of 52 Probands With Primary Obsessive-Compulsive Disorder^a

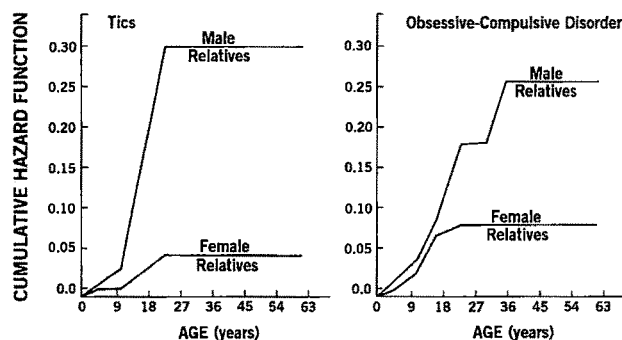
Proband Diagnosis	Relatives With Obsessive-Compulsive Disorder ^b		Relatives With Tics ^{b,c}		Relatives With Tourette's Disorder ^b		Total Relatives Affected ^d	
	N	%	N	%	N	%	N	%
Obsessive-compulsive disorder, no tics	12	16	9	12	1	1	17	23
Age corrected		22		12		1		23
Obsessive-compulsive disorder and tics	7	10	11	15	1	1	14	28
Age corrected		13		15		1		20
Obsessive-compulsive disorder and Tourette's disorder	3	12	4	16	1	4	6	25
Age corrected		16		16		1		24
Total	22	13	24	14	3	6	37	22
Age corrected		17		14		6		22

^aThere were no significant differences in rates of illness in relatives by diagnosis of probands (chi-square or Fisher's exact test).

^bObsessive-compulsive disorder, tic, and Tourette's disorder diagnoses are not mutually exclusive.

^cCategory includes transient and chronic tics and Tourette's disorder.

^dAge-correction factor of tics was used for this category; two age corrections could not be made, and the conservative correction (that of illness with earlier onset) was chosen.

FIGURE 1. Tics and Obsessive-Compulsive Disorder by Age at Onset in 171 First-Degree Relatives of 52 Probands With Obsessive-Compulsive Disorder

tives than female relatives with tics and significantly more male relatives than female relatives with obsessive-compulsive disorder. As shown in table 3, the rates of illness (obsessive-compulsive disorder, tics, or Tourette's disorder) in first-degree relatives did not differ significantly according to proband status (no tics, tics, and Tourette's disorder) by chi-square test.

The Cox proportional hazards model was used to test simultaneously the effects of the probands' sex, age at onset of obsessive-compulsive disorder, comorbid attention deficit hyperactivity disorder, severity of obsessive-compulsive disorder, and severity of tics and the effects of the sex of the relative on the survival function (not having a diagnosis) of the relative. Testing each variable alone on this cumulative hazard function, we found that the only covariate with a significant impact on illness in the relative was the sex of the relative (obsessive-compulsive disorder, $\chi^2=4.67$, $df=1$, $p<0.03$; tics, $\chi^2=13.46$, $df=1$, $p=0.002$; obsessive-compulsive disorder or tics, $\chi^2=12.73$, $df=1$, $p=0.0004$). The cumulative effect of the five proband variables combined

failed as an overall regression model to make a statistically significant contribution to the hazard function (illness in the relative). Thus, of the six variables tested, only the sex of the relative was important in predicting the relative's possible development of tics and/or obsessive-compulsive disorder.

As a further confirmation, the Mantel-Cox statistic in life table analyses was used to compare male and female relatives on the cumulative hazard function (probability of developing tics or obsessive-compulsive disorder by a certain age). Male relatives were found to have a greater risk of both tics (Mantel-Cox statistic=13.83, $df=1$, $p=0.0002$) and obsessive-compulsive disorder (Mantel-Cox statistic=4.91, $df=1$, $p=0.03$) (figure 1). Similar results were obtained for developing either tics or obsessive-compulsive disorder when these were combined into a single analysis.

DISCUSSION

In this study, which addressed the question of the prevalence of Tourette's disorder and tics in child patients with obsessive-compulsive disorder and in their first-degree relatives, 59% ($N=32$) of the 54 subjects had lifetime histories of tics when evaluated at follow-up, although only one-third ($N=17$) actually had a current diagnosis. Methodological difficulties have led to widely varying estimates of the rate of tics and Tourette's disorder in the general population (11–18), so without systematic population studies, direct comparisons of our study group's rates with expected rates are not possible. However, the 11%–15% lifetime prevalence of Tourette's disorder in the patients with obsessive-compulsive disorder and the 1.8% rate in their first-degree relatives is higher than the published estimates of 0.03%–0.40% (11–13). Similarly, the lifetime rates of tics in the patients with obsessive-compulsive

disorder (59%) and their first-degree relatives (14%) are outside the reported range of 4%–12% (14–18). This seemingly high rate of tics and Tourette's disorder among the probands and their first-degree relatives lends support to the hypothesis that some cases of obsessive-compulsive disorder and Tourette's disorder may be etiologically related.

Illness (obsessive-compulsive disorder, Tourette's disorder, and/or tics) in the first-degree relatives was not related to either the sex or the tic status of the obsessive-compulsive disorder probands. This finding is consistent with that of Pauls et al. (10) among families of probands with Tourette's disorder; these authors reported that obsessive-compulsive disorder in the relatives was independent of the sex and diagnosis (with or without obsessive-compulsive disorder) of the proband with Tourette's disorder. In our current study, the male first-degree relatives had a higher rate of tics and of obsessive-compulsive disorder than did the female relatives. In contrast, Pauls et al. (10) reported that male relatives were more likely to have Tourette's disorder, and female relatives were more likely to have obsessive-compulsive disorder without tics, suggesting that obsessive-compulsive disorder could represent the part of the Tourette's disorder spectrum that is more frequently expressed in females. This difference between studies might be explained by the smaller number of families evaluated in our study or by the difference in proband status (obsessive-compulsive disorder versus Tourette's disorder).

A major limitation of the family portion of this report is that our data may underestimate the rate of tics. Although all relatives were seen in person and assessed for the presence/absence of tics, the reevaluation in person with a structured instrument was not done with every relative. Childhood tics that had subsequently resolved may not have been remembered by adults. Thus, if tics were not reported by the patient or family members and had gone "unnoticed" by the interviewer, they would not have been included.

It was hypothesized that at follow-up, some of the probands with obsessive-compulsive disorder might have "developed" Tourette's disorder, given the reported association between Tourette's disorder and obsessive-compulsive disorder and the presence of tics at baseline. Indeed, six males (11%) of 54 patients with obsessive-compulsive disorder who did not meet diagnostic criteria for Tourette's disorder at baseline did so at follow-up. Although it is not surprising that children with tics (who had not passed through their risk period) might subsequently develop Tourette's disorder, the presence of Tourette's disorder in 11% of the subjects seems high, particularly in light of the initial exclusionary criteria.

What distinguished the patients with obsessive-compulsive disorder and Tourette's disorder from those without Tourette's disorder? Only early age at onset of obsessive-compulsive disorder and male sex predicted who might develop Tourette's disorder. This is in keeping with the known predominance in males and the pos-

tulated sex-influenced genetic expressivity (3). Although we previously reported that the age at onset of obsessive-compulsive disorder was lower for boys than for girls (36), the significance of the earlier onset of obsessive-compulsive disorder in the patients with Tourette's disorder is not clear and has not been previously reported.

The patients with obsessive-compulsive disorder and Tourette's disorder were not distinguishable by the nature of their obsessions or compulsions. In general, the obsessive-compulsive symptoms were those typically seen, but a few patients exhibited behavior that was difficult to categorize as a ritual or tic. The categorization of the behavior was based on its complexity and the presence/absence of cognition preceding the action. Typically, a ritual is performed in response to a specific thought and a tic in response to an urge. Behaviors which remained difficult to classify clearly included that of a boy who would spit after the thought that his mouth had become contaminated by human body fluids and that of another patient who "compulsively" bounced a ball and touched his fingers in a rhythmic fashion because his "bones made him do it." Even if obsessive-compulsive disorder and Tourette's disorder are different manifestations of the same underlying illness, it appears that tics and rituals are for the most part clinically distinct and distinguishable. There may be a spectrum of behaviors, ranging from the classical tics of patients with Tourette's disorder to a mixed picture of tics and rituals to clear-cut rituals. Although this set of data does not help us truly address the distinction between tics and rituals, the clinical picture of obsessive-compulsive disorder was essentially not different among the probands with obsessive-compulsive disorder with and without Tourette's disorder.

An earlier age at onset of obsessive-compulsive disorder, a higher baseline anxiety rating (although not a *DSM-III-R* anxiety diagnosis), and a higher CSF 5-HIAA/HVA ratio distinguished the patients with obsessive-compulsive disorder and tic disorders from those without such a comorbid diagnosis. The meaning of the association between anxiety and tics is unclear, as the relation between anxiety and Tourette's disorder has not been systematically studied, and there was no increase in the number of individuals with anxiety disorders—just an increase in the anxiety rating. Perhaps anxiety and tics exacerbate each other or, less likely, they could both be manifestations of the underlying illness.

The increased CSF 5-HIAA/HVA ratio in the patients with obsessive-compulsive disorder and tics is consistent with hypotheses of altered neurotransmitters in Tourette's disorder and obsessive-compulsive disorder (24, 37–39). The present findings are in the same direction as those reported by Cohen et al. (37) for a group of six patients with Tourette's disorder who had a (non-significantly) higher 5-HIAA/HVA ratio than did a comparison group of eight patients with medical disorders. Although our patients with Tourette's disorder had a higher CSF 5-HIAA/HVA ratio than that of the male chronic and transient tic group (N=11), which in

turn was higher than that of the group without tics (N=12), none of these differences was significant. Only three of our eight patients with Tourette's disorder had lumbar punctures, so the small size of the study group may have contributed to the lack of a significant difference. Although no conclusions can be drawn from these nonsignificant results from a small number of subjects, it is tempting to speculate that tics and Tourette's disorder may be associated with disturbances of the serotonin/dopamine ratio.

This is the first large, systematic family study of tics and Tourette's disorder among probands with obsessive-compulsive disorder and their first-degree relatives. The high rate of tics and Tourette's disorder in the 54 patients with obsessive-compulsive disorder is consistent with the previously reported frequent association of these disorders. The apparent high rate of obsessive-compulsive disorder and tics in the first-degree relatives of the probands, independent of the probands' tic status, supports the hypothesis (3, 10) that in some cases, obsessive-compulsive disorder and Tourette's disorder may be alternative manifestations of the same underlying (genetic) illness. Even if the same etiologic mechanism may be responsible for some cases of Tourette's disorder and obsessive-compulsive disorder, the clinical picture of obsessive-compulsive disorder was indistinguishable among those with and without a comorbid tic diagnosis.

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Differences in Neuropsychological and Academic Achievement Between Adolescent Delinquents and Status Offenders

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***Objective:** This study sought to determine whether neurocognitive factors could discriminate delinquents brought before a juvenile court in a large urban area from nondelinquent status offenders brought before the same court. **Method:** Psychological tests were administered to 216 adolescents, aged 13–15 years, presenting to a large urban juvenile court. One hundred ten delinquents (65 male and 45 female) were compared to 106 high-risk nondelinquents (65 male and 41 female) on the WISC-R subtests, the Wide Range Achievement Test, and the Memory for Designs Test. **Results:** Discriminant analysis revealed that the male delinquents could not be discriminated from the comparison group of male status offenders on the basis of scores on any of the measures. Among the female subjects, scores on reading, arithmetic, digit span, and picture completion subtests and the Memory for Designs Test differed significantly between groups, with some of the findings favoring status offenders and others favoring delinquents. **Conclusions:** Overall, the findings did not support the hypothesis that inferior intelligence is an independent risk factor for delinquent behavior.*

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This study tested whether neurocognitive factors played a unique and significant role in predicting delinquent behavior in a group of high-risk, inner-city adolescents. Previous work has shown that delinquents have difficulty with numerous cognitive tasks, and some investigators have interpreted such findings to mean that neurocognitive deficits are implicated in the etiology of delinquency.

In an earlier study (1), the authors reported that delinquents presented with an average IQ deficit of one-half of a standard deviation (approximately 8 IQ points). Further research has indicated that delinquents exhibit deficits in IQ and other cognitive areas, regardless of race (2, 3) or social class (3–6). Moreover, the link between IQ and delinquency has been found in both retrospective and prospective studies (5–8) and across cultures. One retrospective study (8), based on 102 files randomly selected from a family court mental health clinic, revealed that one-third of the delinquent subjects were functioning in the “mentally defective

range” and one-third in the “low average to average range.” A prospective study of children (9) showed that self-reported delinquents had lower IQs than did nondelinquents. Self-report data also indicate that lower IQs and/or poor school achievement antedate the onset of delinquent behavior (7, 10, 11).

There is evidence to suggest that the lower IQs of delinquents are not merely the result of invalid or inappropriate testing. An analysis of male delinquents’ performance on the WISC-R revealed an acceptable level of internal consistency (12). Moreover, WISC-R subtest scores proved to be stable in a sample of children obtained from a juvenile court (13). After examining the factor structure of delinquents’ scores on the WISC-R subtests, investigators in one study concluded that differences in performance between delinquent and nondelinquent males “cannot be attributed to underlying ability structure” (14) and appeared to represent actual differences in cognitive performance capacities.

Delinquents exhibit a tendency to achieve higher scores on performance IQ than on verbal IQ. Previous research found that 70% of delinquent subjects had higher scores on the performance section of the WISC-R than on the verbal section (15). Moreover, hemispheric laterality, as measured by differences in verbal and performance scores, has been found to be related to delinquency (16). This phenomenon appears to have been related to the persistence of delinquent behavior among a group of 78 female delinquents whose cases had been tried in court; the rate of recidivism was found

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to be significantly higher when performance IQ was greater than verbal IQ (17).

Studies associating neurocognitive deficits with delinquent behavior have not been limited to IQ testing. It has been reported that among male juvenile delinquents, auditory processing deficits and articulation disorders are common (60%) (18). Another study found deficits in academic skills to be among the most impressive covariates of antisocial behavior (19). Moreover, high rates of attention deficit disorder have been found among delinquents; the impaired capacity for sustained attention and concentration associated with this disorder has consistently been identified as an important risk factor for the development of conduct disorder and delinquent behavior (20–23). Finally, it has been reported that delinquents, with or without a history of attention deficit disorder, score significantly lower than nondelinquents on verbal, visual-spatial, and visual-motor integration skills (24).

A previous study (5) discerned a pattern among studies concerning neurocognitive factors and delinquency. The authors pointed out that "the functions most consistently cited as impaired have been verbal and executive (abstraction, planning, inhibition of inappropriate responses, mental flexibility, sequencing, attention, and concentration)," although relative memory deficits have been cited as well. They concluded that the consistency of findings "has been impressive and suggests a robust effect."

The etiology of the link between neurocognitive factors and delinquent behavior has been the subject of considerable speculation. Theoretical models, developed primarily from studies of antisocial adults, have proposed that neuropsychological factors, such as diminished autonomic reactivity with resulting "stimulus seeking" (25–28), may contribute to the development of antisocial and/or criminal behavior. Such behavior has also been attributed to impaired passive-avoidance learning patterns (29, 30) or a combination of neurological and developmental factors (31).

Another approach has been to emphasize the fact that neurocognitive deficits contribute to a variety of childhood problems and negative experiences which may function as risk factors for delinquent behavior during adolescence. These problems include school failure (3, 32), poor reading skills (33), impaired internalization of verbally mediated controls (34, 35), early alcohol use (36, 37), and poor peer relationships (38–40). Stressing that delinquency results from complex interactions among a number of variables, theorists such as Lewis (41) and Levine (42) have included neurological impairment as one of several risk factors in their models of aggressive delinquent behavior. In spite of the findings reviewed here and the theories that seek to explain them, some studies of this subject have failed to find a link between neurocognitive status and delinquency. One study followed children between the ages of 8 and 12 who had been classified as learning disabled, and no association was found between their neurological disorders and subsequent delinquent behavior during ado-

lescence and early adulthood (43). Moreover, an investigation of juvenile violent, nonviolent, and sexual offenders found no relation between neurocognitive profiles and the severity of violent behavior (44). Other studies (45, 46) have suggested that socioeconomic factors and family problems may account for the apparent relation between academic problems and delinquency.

Comparisons among the studies on this subject are difficult, since a variety of measures and methods of data analysis have been used, and groups representing differing degrees of antisocial behavior and/or delinquency have been compared with various "normal" groups. In many of these studies, the assessment of the effects of neurocognitive factors has been confounded by the fact that the delinquent groups have differed from the comparison groups on many potential risk factors, some of which may have mediated the apparent relation between neurocognitive status and delinquent behavior. Thus, although a majority of the evidence we have just reviewed indicates that delinquent behavior is correlated with neurocognitive deficits, it is not clear whether these deficits contribute directly to the etiology of delinquency or whether the relationship is mediated by environmental factors.

Much of the literature on this subject refers to "antisocial" behavior, without making consistent distinctions between criminal and noncriminal types of obdurate behavior. In legal terms, "delinquent" acts are those against property or persons which, if committed by an adult, would constitute misdemeanors or felony criminal offenses. In contrast, "status offenses" are acts that are considered inappropriate or annoying when committed by minors (truancy, running away, stubbornness, and disobedience) but that would not ordinarily constitute a violation of law if committed by an adult.

This study sought to determine whether neurocognitive factors can discriminate delinquents brought before a juvenile court in a large urban area from status offenders brought before the same court. Such a discrimination would indicate that neurocognitive factors are implicated in the distinction between the criminal and noncriminal members of a group of "antisocial" adolescents who share a common, high-risk environment and a proclivity toward problem behavior. This would be consistent with the hypothesis that deficits in IQ and/or neurocognitive performance serve as independent risk factors for criminal behavior rather than as markers for environmental factors which mediate their relationship with delinquency.

A further aim of this study was to determine whether, in an inner-city population at high risk for delinquency, there are gender differences in the manner in which neurocognitive factors act as risk factors for delinquency. Previous research has tended to focus on males, who are overrepresented among delinquent adolescents. No previous studies have compared the contributions of neurocognitive factors to male and female delinquency and used the type of comparison group that was used in this investigation.

METHOD

The study group included 216 adolescents (130 male and 86 female) referred to a large inner-city juvenile court clinic. All data were gathered by sequential chart review of records completed between 1983 and 1987. The records of all adolescents between the ages of 13 and 15 years were included in the study. Each of the 216 adolescents whose cases were represented in this study had been referred to the juvenile court's mental health clinic for psychometric testing. The reasons for referral were varied, including assessment of 1) diagnosis, 2) competency to stand trial, 3) appropriate school placement, 4) potential for harming self or others, 5) child abuse and neglect, 6) appropriate living arrangements, and 7) overall neurocognitive status. In addition to the psychometric testing, all adolescents received a clinical psychiatric interview.

The psychometric test battery always included the Wechsler Intelligence Scale for Children—Revised (WISC-R) (47), the Wide Range Achievement Test—Revised, Second Version (WRAT-R-II) (48), and the Memory for Designs Test—Revised (49). Additional tests, such as the Rey-Osterrieth Complex Figure Test (50), the Bender Gestalt (51), and the Hooper Visual Organization Test (52), were used as clinically appropriate during the study period. The 216 study subjects represent all for whom at least the WISC-R, the WRAT-R-II, and the Memory for Designs Test were completed and documented in the court records.

For the purposes of analysis, the subjects were divided into two groups: delinquents (N=110, 65 male and 45 female) and status offenders (N=106, 65 male and 41 female). Group membership was determined by the presence or absence of criminal conduct. The legal definitions of the two groups are as follows. A delinquent is defined as "a child between the ages of 7 and 17 who violates any city ordinance or town by-law or commits any offense against the law of the Commonwealth" (53). A status offender is an adolescent brought before the court on a petition seeking determination of whether he or she is "in need of services." The wording defining the legal status of such a petition is, "A parent or legal guardian of a child having custody of such child . . . may apply for a petition . . . alleging that said child persistently runs away from home or persistently refuses to obey the lawful and reasonable commands of said parents" or alleging "guardian's inability to adequately care for and protect said child" (54).

While truancy, running away, or "disobedience" may be perceived as "socially deviant" by some, such behavior is meaningfully distinguished from armed robbery, rape, or assault. Socially deviant behavior is a continuum, but one clear line is the difference between criminal and noncriminal behavior. In our society, the presence or absence of known criminal conduct is an extremely important developmental and social factor. While there might have been some within-group differences, the purpose of conducting this large group study was to

permit an investigation and comparison of group characteristics.

The ethnic composition of the 216 subjects was as follows: approximately 50% were black, 37% were white, 10% were Hispanic, and 4% came from other ethnic groups. A chi-square test revealed no significant difference in race/ethnicity between the delinquents and the status offenders. Fifty-four percent of the subjects were eligible for Medicaid; a chi-square analysis showed that the groups did not differ significantly in this regard.

In this study, the two groups were homogeneous in terms of specific geographic location, race, gender, age, and income status. The standard measurements used in the analysis have considerable reliability and validity insulation from "environmental" characteristics. Also, the extent to which factors such as income level, educational system, or race may have an impact on scores was moderated by the use of groups with substantially homogeneous socioeconomic status.

There might be individual and family factors that were not addressed by our study method but that are potentially important in the understanding of delinquency. These might include psychiatric diagnosis and family constellation. However, the measures we used remain valid and reliable across individual psychopathology and family constellation. The literature supports the existence of effects of differences in education, race, and income on standardized measures, and these were controlled for in this study.

RESULTS

Table 1 presents the results of a series of two-way analyses of variance (ANOVA) in which group (delinquents versus status offenders) and gender served as between-subject factors. Dependent variables consisted of scores on each subtest of the WISC-R, standardized scores on reading, spelling, and arithmetic from the WRAT-R-II, and the corrected score from the Memory for Designs Test. Scores on each of these measures are standardized with respect to age. The results of these univariate analyses yielded marginally significant group effects on the information, vocabulary, and comprehension subtests of the WISC-R, with the status offenders having the higher scores. The delinquents had higher scores on the digit span subtest and the Memory for Designs Test, although a higher score on the latter represents poorer performance and the possibility of organic dysfunction.

Statistically significant gender differences were observed on the picture completion and object assembly subtests of the WISC-R; the males exhibited superior performance. The males also showed marginally higher scores on the block design subtest. The females performed significantly better than the males on the coding subtest and the digit span subtest of the WISC-R, as well as the reading, spelling, and arithmetic subtests of the WRAT-R-II. A marginally significant Group by

TABLE 1. Scores on Psychometric Tests of 216 Adolescents Referred to a Juvenile Court Clinic

Test/Subtest	Nondelinquent Status Offenders					Delinquents					Mean Score of Total Study Group		ANOVA Probability (p)		
	Males		Females		Total	Males		Females		Total			Group	Gender	Group by Gender
	N	Mean	N	Mean		Mean	N	Mean	N		Mean	Mean			
		Score		Score	Score			Score		Score					
WISC-R															
Information	61	6.93	45	6.96	6.94	65	6.58	45	5.87	6.29	6.75	6.41	0.07	0.37	0.34
Similarities	61	8.21	45	8.40	8.29	65	8.21	45	7.44	7.90	8.21	7.92	0.25	0.48	0.25
Arithmetic	61	7.90	45	8.11	7.99	65	7.85	45	7.89	7.86	7.87	8.00	0.71	0.73	0.82
Vocabulary	61	7.28	45	7.89	7.54	65	6.95	45	6.82	6.90	7.11	7.36	0.06	0.52	0.31
Comprehension	61	7.67	45	8.07	7.84	65	7.29	45	7.02	7.18	7.48	7.54	0.37	0.87	0.40
Picture completion	61	10.30	45	8.53	9.55	65	9.86	45	8.56	9.32	10.07	8.54	0.59	0.0001	0.55
Picture arrangement	61	10.43	45	10.04	10.26	65	9.80	45	9.87	9.83	10.10	9.96	0.30	0.69	0.57
Block design	61	8.78	45	8.53	8.68	65	8.80	45	7.69	8.35	8.79	8.11	0.31	0.10	0.29
Object assembly	61	9.97	45	8.62	9.40	65	9.49	45	8.42	9.05	9.72	8.52	0.46	0.008	0.76
Digit span	54	7.44	38	8.58	7.91	56	8.23	35	9.29	8.64	7.85	8.92	0.10	0.02	0.93
Coding	60	7.53	45	8.84	8.10	65	7.14	45	9.76	8.21	7.33	9.30	0.52	0.0001	0.11
Full-scale IQ		89.11		88.69	88.93		86.94		85.58	86.38	87.99	87.13	0.17	0.64	0.81
Wide Range Achievement Test															
Reading	54	83.91	40	94.90	88.59	55	87.65	41	88.07	87.83	85.80	91.44	0.57	0.04	0.05
Spelling	54	80.57	40	90.90	88.59	55	82.47	41	85.96	83.95	81.53	88.40	0.50	0.003	0.13
Arithmetic	54	73.60	40	78.48	75.67	55	74.53	41	76.93	75.55	74.06	77.69	0.86	0.04	0.49
Memory for Designs Test	43	0.68	33	0.58	0.64	51	0.96	34	1.68	1.25	0.84	1.13	0.07	0.43	0.26

Gender interaction was observed on the reading subtest of the WRAT-R-II, reflecting the fact that females outperformed males by 11 points in the status offender group, while the gender difference in the delinquent group was less than one-half of a point. No significant Group by Gender interactions occurred on the other variables.

There were no significant gender or group differences in full-scale IQ. This indicates that although skills and achievement differed in specific areas, the groups were well matched in terms of overall intellectual ability as measured by the WISC-R. Power calculations revealed that, given the sample size and an alpha level of 0.05, a difference of 8 IQ points could have been detected with a probability of 0.99 if such a difference existed.

The multivariate relationships between cognitive performance and group (delinquents versus status offenders) were examined by means of two stepwise discriminant analyses, one for the male and one for the female subjects. The cognitive variables from the WISC-R, the WRAT-R-II, and the Memory for Designs Test served as predictors, with group classification as outcome. Table 2 shows that the strength of the relation between cognitive performance and group classification varied markedly as a function of gender. For the male subjects this relationship proved to be so weak that no variables would have been included in the model if the 0.05 level of significance had been used as the inclusion criterion. In contrast, strong relations between predictors and outcome were observed for the female subjects. In order to determine whether the predictors combined in similar ways to predict male and female delinquent classification, a lenient inclusion criterion of $p=0.15$ was used, thus allowing marginally

significant variables to enter the model and providing a tentative assessment of the combined cognitive determinants of male delinquent status.

For the male subjects, only two variables (scores on the digit span subtest and the Memory for Designs Test) made even marginally significant contributions toward predicting group membership. The model consisting of these two variables fell short of statistical significance ($p=0.079$), with a canonical correlation of 0.26. In this model the delinquents were characterized by better digit span scores but greater difficulty with the Memory for Designs Test. Classification results revealed that only 55% ($N=82$) of the male subjects were correctly classified by this model, with 49% ($N=43$) of the delinquents and 62% ($N=39$) of the status offenders assigned to the correct groups.

For the female subjects, cognitive measures predicted group membership with a much greater degree of accuracy. Five variables contributed to the model: scores on the digit span subtest, the picture completion subtest, the WRAT-R-II reading and arithmetic subtests, and the Memory for Designs Test. The final model was statistically significant at the 0.001 level, with a canonical correlation of 0.57. As with the male subjects, delinquency was associated with superior digit span scores but inferior scores on the Memory for Designs Test. In addition, superior performance on the picture completion subtest with inferior performance on the reading and arithmetic subtests contributed toward classification as a female delinquent. Classification results revealed that 76% ($N=55$) of the female subjects were correctly classified by the model, with 75% ($N=28$) of the delinquents and 78% ($N=27$) of the status offenders assigned to the correct groups.

TABLE 2. Discriminant Analyses Predicting Delinquent and Status Offender Classifications for Adolescents Referred to a Juvenile Court Clinic

Item	Male Subjects ^a	Female Subjects ^b
Standardized discriminant coefficient		
Predictor		
WISC-R digit span score	0.83	0.87
Memory for Designs Test corrected score	0.69	0.61
WISC-R picture completion score		0.58
Wide Range Achievement Test reading score		-0.70
Wide Range Achievement Test arithmetic score		-0.43
Group mean		
Delinquents	0.26	0.67
Status offenders	-0.27	-0.69
Analysis of group means		
Wilk's lambda	0.93	0.68
Chi-square	5.07, df=2, p=0.079	19.78, df=5, p=0.001
Canonical correlation	0.26	0.57
Eigenvalue	0.07	0.48

^aN=75 for group on which model was estimated (subjects with complete data on all predictors); N=82 for group used in classification results (subjects with complete data on all variables included in the final model).

^bN=55 for group on which model was estimated (subjects with complete data on all predictors) and for group used in classification results (subjects with complete data on all variables included in the final model).

DISCUSSION

This investigation differed from previous studies in using a comparison group of status offenders whose risk status on environmental and family factors was so similar to that of the delinquents that both groups had actually appeared before the same court. The crucial difference between the groups was that the members of one had been convicted of engaging in criminally delinquent activity, while those of the other had not. This study examined whether cognitive factors played a significant role in determining which adolescents fell into the delinquent group.

The univariate analyses, in which data from male and female subjects were analyzed together, provided only marginal evidence of a link between cognitive performance and delinquency. In these analyses the delinquents displayed superior short-term memory ability (as measured by the digit span subtest) relative to the status offenders. However, they exhibited relatively inferior performance on WISC-R subtests involving long-term memory (vocabulary, comprehension, and information) and showed greater evidence of dysfunction on the Memory for Designs Test.

These initial analyses provided strong evidence of a relation between cognitive performance and gender, with females showing a significantly higher level of performance than males on all three tests of academic achievement and on WISC-R subtests involving short-

term memory and symbol manipulation (digit span and coding). Males, on the other hand, displayed somewhat higher scores on WISC-R subtests involving abstract and/or spatial relationships (picture completion, object assembly, and block design).

In view of these gender effects, the discriminant analyses that examined the overall relation between delinquency and cognitive performance were performed separately for the male and female subjects. These analyses revealed that cognitive factors could discriminate female delinquents from female status offenders with a significant degree of accuracy. Female delinquency proved to be associated with lower achievement in arithmetic and reading, in spite of greater ability in short-term memory (digit span) and sequential reasoning (picture completion). Relatively poor performance on the Memory for Designs Test, which has been linked to organic dysfunction, was also predictive of delinquent status among females.

Since overall IQ was not significantly different between the delinquent and nondelinquent groups, these results cannot be attributed to a global concept of intelligence. Thus, although there were significant differences, they are inconsistent with the notion that inferior intellectual ability is an independent risk factor for delinquency among females. Rather, the pattern describing the intellectual performance of female delinquents appears to be one of underachievement relative to the status offenders.

The results of the discriminant analyses on the male subjects indicated that delinquency could not be predicted with any degree of accuracy on the basis of cognitive performance. Thus, this study provides no evidence to suggest that inferior intellectual ability plays a role in separating delinquent males from a comparison group exposed to the same environmental risk factors. The results of this study are consistent with those of earlier work in finding that delinquent adolescents exhibit a level of cognitive performance that is well below average. However, this study found that a nondelinquent comparison group exposed to the same environmental risk factors exhibited equally poor overall cognitive performance. Furthermore, although some significant group differences were observed, the findings did not suggest that the delinquents were characterized by inferior intellectual ability relative to the comparison group. Thus, when environmental factors are held relatively constant, cognitive deficits do not emerge as an independent risk factor for delinquency.

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Intravenous Versus Intramuscular Atropine in ECT

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Twelve patients receiving ECT consented to random assignment to either intravenous or intramuscular administration of atropine for a total of 48 ECTs. There were no statistically significant differences between routes of administration in heart rate, blood pressures, or sialorrhea, but intravenous administration eliminated one injection per treatment and the development of dry mouth and tachycardia between the intramuscular injection and ECT. The authors recommend that atropine for ECT be administered intravenously.

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Although not a uniform practice, administration of atropine to patients receiving ECT to decrease sialorrhea and prevent vagal-induced bradycardia or asystole is not uncommon (1). Atropine is given either intramuscularly 30 minutes before induction of anesthesia or intravenously 2 minutes before induction of anesthesia. Current practice is to give atropine intramuscularly (2, p. 94). Reduction of sialorrhea is maximized by intramuscular administration. However, given individual differences in distribution and duration of action of atropine, intramuscular administration before anesthesia may offer little protection against bradycardia or asystole in some patients (1).

The purpose of this paper was to compare the intravenous and intramuscular routes of atropine administration in patients receiving ECT.

METHOD

The subjects (N=12) were eight women and four men who were scheduled to receive ECT. Their mean age was 52.3 years (SD=19.2) (range=23-74). They were voluntary psychiatric patients with mixed diagnoses.

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Patients with cardiac pacemakers were excluded from participation in the protocol because administration of atropine before ECT is often contraindicated in such patients. No changes were made in the psychotropic medications that the patients received during the study period. Two patients received tricyclic antidepressants (nortriptyline and amoxapine), two received a neuroleptic with an anticholinergic, one received a neuroleptic with a benzodiazepine, and seven received no psychotropic medication. All patients provided informed consent to their participation in the study.

The route of atropine administration was randomized beginning with the second and ending with the fifth ECT, with the constraint that each patient undergo two intramuscular and two intravenous sessions. The first ECT was not studied due to the elevated anxiety patients typically have before the first treatment. In each of two sessions, intramuscular atropine (1.0 mg) was given in the gluteus muscle 30 minutes before anesthesia induction or intravenous atropine (0.6 mg) was given 2 minutes before anesthesia induction. Anesthesia consisted of methohexital, succinylcholine, and hyperoxygenation. ECT was administered with the MECTA SR-I with bilateral electrode placement.

The ECT nurse, blind to route of atropine administration, recorded blood pressure and heart rate before atropine administration, before methohexital sodium administration, and 5, 15, and 30 minutes after ECT. Level of confusion was clinically assessed globally as present or absent. Post-ECT secretions were categorized by the nonblinded anesthesiologist (A.A.) on a 3-point scale on which 0=not excessive, 1=moderate but requiring no clinical intervention, and 2=copious, requiring clinical intervention.

RESULTS

The 12 patients received a total of 48 study ECTs. Twenty-four treatments followed intramuscular atropine and 24 treatments followed intravenous atropine. Analyses of covariance with repeated measures were used to assess the route of administration (intravenous versus intramuscular) and time (before the administration of methohexital sodium versus 5, 15, and 30 minutes after ECT) with Greenhouse-Geisser adjustments for the degrees of freedom (3). The covariate in each analysis was the value before the administration of atropine, and separate analyses of the systolic and diastolic blood pressure and heart rate were performed. The dependent variables were the means of each subject's blood pressure and heart rate obtained in the two intravenous sessions and in the two intramuscular sessions.

Consistent with the known effects of ECT, significant changes in blood pressure (time main effects: systolic, $F=14.02$, $df=3, 29$, $p<0.01$; diastolic, $F=3.77$, $df=2, 20$, $p<0.05$) and heart rate ($F=5.03$, $df=2, 20$, $p<0.02$) occurred. These consisted of transient increases of blood pressure and heart rate 5 minutes after ECT, followed by gradual reductions to pre-ECT levels approximately 30 minutes after ECT.

The differences between route of administration and blood pressure and heart rate changes following ECT did not attain statistical significance at conventional alpha levels. Two trends, however, were evident. Elevated systolic blood pressure tended to persist after ECT for a longer time period under intravenous than under intramuscular administration (5–30 minutes after ECT) (administration by time interaction, $F=1.93$, $df=2, 25$, $p=0.16$). For heart rate, the increase 5 minutes after ECT tended to be larger under intravenous than under intramuscular administration (administration by time interaction, $F=1.75$, $df=2, 25$, $p=0.19$). Secretions and bradycardia did not differ substantially under intravenous compared with intramuscular administration.

DISCUSSION

There were no statistically significant differences in blood pressure, heart rate, or secretions between intramuscular and intravenous atropine. Although there was a trend for systolic blood pressure elevations to persist longer under intravenous conditions compared with intramuscular, it did not reach statistical significance. Similarly, larger transient heart rate increases occurred 5 minutes after ECT under intravenous than under intramuscular administration, but these differences were not statistically significant.

Because the number of subjects evaluated in the present study was relatively small, the differences that might have occurred in blood pressure, heart rate, and secretions following intravenous, as opposed to intramuscular, atropine administration may not have been sufficient to attain statistical significance. Thus, we can-

not definitively discount the possibility that our failure to document differences between intravenous versus intramuscular administration reflects low statistical power (or, equivalently, that our results contain type II error). In addition, because therapeutic rather than scientific goals had precedence in this study, the anticholinergic properties of the medications that some of the patients received may have reduced the likelihood that statistically significant results would be obtained.

This report does not attempt to resolve the issue of whether atropine should be used in conjunction with ECT. This controversy has existed for a long time. In 1964, Cropper and Hughes (4) questioned the wisdom of "routine" atropine premedication, but the overwhelming larger body of opinion favored its use. The intravenous route provided the maximal vagolytic action at the time of the stimulation. More recently, Wyant and MacDonald (5), among others, have raised questions about the routine use of atropine during ECT. Their patients were receiving unspecified psychotropic medications with an unknown degree of anticholinergic protection. Miller et al. (6) observed less vagal arrhythmias in 44 patients when they received atropine than when they received placebo before ECT. The frequency of ventricular arrhythmias was unaffected. Tachycardia and confusion are known side effects of atropine. Relaxation of the lower esophageal sphincter with the resultant risk of gastroesophageal reflux and aspiration is also of concern.

Clement (7) reported that one out of 100 patients receiving intravenous atropine 75 seconds before ECT had severe bradycardia and that 22 receiving atropine subcutaneously 30 minutes before ECT developed severe bradycardia or asystole. The less efficient vagal blockade may be related to the fact that in a "busy clinic," 30 minutes could be anywhere from 10 to 80 minutes. Patients in that study liked the lack of dry mouth and unpleasant tachycardia before the treatment at a time when anxiety was high and they could not be premedicated.

A standard anesthesia text states, "Prevention of reflex bradycardia seems unlikely with the timing and dose of intramuscular anticholinergic typically administered for preoperative medication" (8, p. 388). Rich et al. (9) recommended a subcutaneous dose of 1.0 mg of atropine because they noted no change in ECG abnormalities following doses ranging from 1.0 to 2.5 mg. Hence, there was no advantage of higher doses.

CONCLUSIONS

Three procedural factors favor intravenous over intramuscular administration of atropine. First, intravenous atropine administration permits more accurate estimation of the time of its effects than does intramuscular administration. This is important because in clinical settings, many external factors can lengthen or shorten the time interval from the intramuscular atropine until the ECT. Second, patient comfort is greater with intravenous atropine. The 30-minute interval before the ECT is a period of

great anxiety for many patients, and the tachycardia and dry mouth that patients experience during this interval with intramuscular atropine can exacerbate their anxiety. Third, there are twice as many punctures with intramuscular than with intravenous administration because the latter can be given through the same intravenous line as the anesthesia. In addition to reducing the patient's pain, the intravenous administration lessens the chances of injury and work for the staff.

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Book Forum

Nancy C. Andreasen, M.D., Ph.D., Editor

LEADERS AND THINKERS

Working With Dr. Schweitzer, by Louise Jilek-Aall, M.D. Blaine, Wash., Hancock House, 1990, 208 pp., \$16.95 (paper).

"Schweitzer, Albert, Alsatian physician, philosopher, theologian, and musician, in French Africa, 1875-1965." This is how the name index of my dictionary sums up the life of one of the most remarkable men of the twentieth century, a man called a saint by some and a self-righteous tyrant by others. As a physician he made no great medical discoveries but, rather, established a modest hospital in 1913 in the backwater village of Lambaréné in Gabon, West Africa. As a philosopher he expressed an optimistic belief that nature was indifferent and that each person had a duty to bring some portion of the misery in the world to an end. As a theologian he wrote shocking psychiatric and historical studies of Jesus but found personal strength and guidance in the Christian message of love. As a musician he was a biographer of Bach and an accomplished organist.

In 1954 Dr. Schweitzer went to Oslo to receive the Nobel Peace Prize. A torchlight procession was led by medical students from the old university to the city hall. When the laureate and his wife stepped out onto the balcony, they were greeted by 20,000 well-wishers who spontaneously expressed their warm feelings by singing an old Norwegian hymn. Louise Aall, a premedical student, was in the throng. Seven years later she was toiling with her hero in the tropical heat.

Louise Aall studied tropical medicine in Switzerland before working as a bush doctor in Tanganyika (now Tanzania). In 1960, at the request of the International Red Cross, she worked in the war-ravaged Congo. A year later, exhausted from work, she planned a leisurely vacation by boat around Africa back to Tanganyika. While waiting for her boat she decided to fly to Lambaréné for a brief visit.

Dr. Schweitzer's hospital, famous throughout the world, was nothing more than a series of wooden buildings with rusted iron roofs. Dr. Aall introduced herself to Mlle. Mathilde Kothmann, the secretary whose approval was necessary for anyone desiring to meet Dr. Schweitzer, and that evening Dr. Aall was invited to dine with the good doctor. Dr. Schweitzer sat at the center of a long table with hospital physicians to his right and nurses to his left. Guests were seated on the other side of the table. Dr. Aall was given the most privileged position, opposite the 86-year-old physician. It was a magical event. After the meal Dr. Schweitzer pushed aside the plates, read a passage from a huge Bible, and discoursed on the apostles' reaction to the death of Jesus. He then walked to a piano and played several sing-along tunes as well as his own compositions. Suddenly he said, "That's enough for today. Good night."

Dr. Aall stayed in the staff quarters, which had no electricity or running water. Mosquito screens took the place of walls in the front and back of the building, "a thin and fragile barrier

between oneself and the untamed nature outside." That night and almost every night thereafter she was lulled to sleep by the crystal clear melodies of Bach that came from Schweitzer's organ.

A measles epidemic was raging, and Dr. Aall could not resist the invitation to work at the hospital. Soon she was surrounded by coughing, moaning, and dying children. Dr. Schweitzer sat at a large table in the center of the clinic and, amid the turmoil, wrote letters and prepared the evening's lecture while overseeing the clinical work and offering advice in difficult situations. The operating room presented special problems at times. Once a lizard, overcome by ether vapors, fell from the ceiling into a patient's abdomen. Another time, to save a patient with a ruptured ectopic pregnancy who was bleeding dangerously, Dr. Aall, using a strainer and anticoagulant, scooped up the blood from the patient's abdomen and infused it back into her through an arm vein. The woman recovered without any complications.

Plane loads of tourists would descend on the hospital, interfering with patient care. "We loathed the questions of these tired-looking travelers who seemed to always be in such a hurry and never took time to listen to our answers. Equipped with a camera, they hunted for something to shoot, thoughtlessly photographing patients in pain, and even dying patients." Dr. Schweitzer's favorite visitor, however, was Marie-Anne. "This extraordinary lady was of the type men only like when her charm and caprices are for them exclusively and whom women, especially hard-working ones, find difficult to tolerate." Dr. Aall was asked to take the lady on a boat trip with oarsmen from the leprosy compound. Marie-Anne took umbrage on this trip and, insulted, shortened her visit, giving Dr. Aall "an indelicate souvenir selected in a vengeful mood." Intrigued, I called Dr. Aall but she would not reveal what the present was, although she did indicate it was quite gross and said, "Who but Dr. Schweitzer could appreciate Marie-Anne?"

Mentally ill patients were cared for by Dr. Friedman, a Jewish doctor who had survived the Nazi concentration camps. When a servant became ferociously paranoid, Dr. Aall insisted he be brought to a special compound, where he was locked in an empty, windowless room (a heavy wooden grill on the door allowed in light and fresh air) that was "built solid enough to withstand the onslaught of even the most violent psychiatric patient." Despite incessant use of medication the patient worsened. His family, convinced that he was possessed by demons, talked of releasing the demon by making a hole in his chest. Dr. Schweitzer would have none of this, however, and went to the patient and said, "It's enough! You have shown us your sorrow and you went to the limits of what a human can endure. Nobody wants to harm you; we all wish you to be with us. Come back to us or you will die. To atone for what you did to your wife, you have to live! Show us that you are a man of courage as well as a man of heart." With those words the spell was broken and the patient recovered.

Dr. Jilek-Aall has filled the pages of this upbeat, tender book with lively anecdotes about the everyday life of Dr. Schweitzer, bowed by age but unyielding in his humanity. Although many books have been written about Lambaréné, this one stands out for its vivid simplicity and insights into the customs, mentality, and relationships of those who worked under the tutelage of this great old man of Africa.

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Looking Back: Memoirs, by Lou Andreas-Salomé; edited by Ernst Pfeiffer; translated by Breon Mitchell. New York, Paragon House, 1991, 226 pp., \$18.95.

Alluring to men and compassionate with women, Lou Andreas-Salomé (1861–1934) cut a wide swath across the intellectual terrain on both sides of the artificial divider called *fin-de-siècle*. Among her most notable conquests were Nietzsche, Rilke, and the Freuds (both Anna and Sigmund). Her marriage remained unconsummated while she sought the companionship of numerous “lovers”—how overtly sexual they were is not disclosed. Her primary love was self-centered: “I intend to shape my life for myself, no matter how it turns out.” Her memoirs are like inner dialogues, exasperatingly verbose, but they reveal a wonderfully complex, unconventional, feminist mentality.

Louise von Salomé grew up in St. Petersburg, the last of six children and the only girl, pampered by her Russian servants, adored by her brothers and her elderly father, a German-Baltic military officer. Her mother was “not a natural friend.” Lou was an adolescent when her father died. Almost immediately she attached herself passionately to a Dutch Protestant cleric, Hendrik Gillot, who reciprocated her love and offered to abandon his wife and children to marry her. They did not marry, but he instructed her in philosophy and converted her to his faith. “Now all loneliness is at an end . . . he is He,” she writes. This blend of spiritual and erotic ecstasy was to characterize all of her subsequent love affairs.

Gillot, for whom she wrote sermons, officiated at her marriage at age 25 to the brilliant but rather disorganized Karl Andreas, a professor of Oriental and Indo-European languages who was 15 years her senior. There was illness on both sides. Lou was exceedingly “nervous,” coughed blood, and sought treatment at various spas. Karl attempted suicide by stabbing himself in the chest the night before the engagement. He nearly died. Their marriage of convenience gave him security for his scholarship and provided a home base for her notorious adventures. Before and after the marriage, Lou lived and traveled with Paul Rée, a brilliant young philosopher and medical student, joined from time to time by the charismatic Nietzsche, who allegedly also wanted to marry her. “What does it mean to get close to a person?” she asks, and answers, “a coming together that takes us somewhere we didn’t expect to go: one of those precious relationships that falls outside the realm of what can be precisely analyzed.”

Her most intense and stressful relationship by far was with Rainer Maria Rilke. “His identification with everything misbegotten and rejected becomes an absolute part of his emotional makeup, in a manner which probably occurs only in a creator unable to create.” To help him overcome his work inhibition, she took him to her native Russia, twice visited Tolstoy, and wrote poetry for and with him. “We were but a single person.” Rilke’s profound anxiety, restlessness, impatience, self-debasement, preoccupation with death and the oc-

cult, morbid sensitivity, distorted body image, and tendency to throw himself to the ground in frustration suggests a borderline personality. Lou thought of him as “the first truly real person in my life,” but later regretted having lacked the necessary clinical skills to treat him properly.

She sought training first with Adler, then with Sigmund Freud, and from psychoanalysis acquired “the tendency not to allow oneself to be distracted by general considerations about whether the end results are pleasing or not, to focus totally on the precise investigation of the object and the special case, whatever the outcome might be.” She muses on the meaning of sublimation: “Even the most forbidden sexual perversions, ‘in spite of their abominable effects,’ could be termed sublimations—in that, fixated at the infantile stage of sexuality, they remained diversions from the goal of physical maturity.” On Freud: “It was his rational approach to scientific research which yielded the discovery of the irrational at the end of the path he followed so unflinchingly.” Meetings of the Vienna Psychoanalytic Society felt to her “like a gathering of brothers and sisters.” She last visited Freud in 1928. Two years later her husband died at age 84. Her remaining years were spent seeing patients, reminiscing about herself and the men in her life, and writing. Altogether she produced 17 books, including novels, collections of short stories, plays, poems (some are reproduced in this book), a monograph on “The Erotic,” and psychoanalytic essays.

Her memoirs have appeared in three German editions since 1951, but this is the first English translation. It is done with great thoroughness and includes 62 pages of notes by the editor, a personal friend to whom Lou bequeathed all of her papers. This is a book for specialists and literary scholars, but whoever reads it will be touched by the author’s rare inner vision and astonishing intellect. Her conclusion, in facing death, is that “existence remains for me a picture puzzle: and yet we too are included within its open secret.”

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Vygotsky’s Psychology: A Biography of Ideas, by Alex Kozulin. Cambridge, Mass., Harvard University Press, 1991, 279 pp., \$29.95.

Along with Luria, Lev Vygotsky has been the leading intellectual force in Soviet psychology. His activities were limited to approximately 20 years (1916–1934) and were suppressed during much of this time because he did not readily conform to the prevailing and all-encompassing Marxist ideology (talk about “political correctness”). The author, a Moscow-born physician who teaches psychology at Boston University, has attempted to summarize Vygotsky’s work and to place it in the larger context of postrevolutionary politics in Soviet Russia and Vygotsky’s relationships with other Russian and Western thinkers.

This book may have tried to accomplish too much. For instance, in just a few pages one finds aesthetic theory, psychoanalysis, Hegelian philosophy, and Marxist theory interwoven with neuropsychology, psychiatry, and child development. Although this range of topics reflects the broad interests of Vygotsky himself, I think the book would have benefited from a more critical review of those domains of Vygotsky’s scientific work which could be evaluated in terms of the empirical findings of his group and other researchers both past and present. Instead, the book, at least in part, seems implicitly devoted to demonstrating that Vygotsky not only

directly influenced—and was influenced by—a large number of individuals but also presaged the bulk of enlightened psychological research of the twentieth century. Leaving aside the merits of this claim, it requires the author to review the writings of a large number of other scholars, such as Piaget, Luria, Leontiev (Vygotsky's student), Bakhtin (the Russian philosopher and philologist), Heinz Werner (the German-American developmental psychologist), and Freud, just to name a few. This leaves the reader with a potpourri of rather abstract summaries of ideas that are dense and, at times, difficult to digest, in contrast to Vygotsky's translated writing, which is lucid, provocative, and always refreshingly "close to the data" of actual subjects.

A series of principles and assumptions are highlighted—that actions are precursors to thought, that human intelligence is highly social in origin, and that language is the plinth of human consciousness. There is, however, no critical evaluation of these points of view. Perhaps this is acceptable for a book that is intended to be a kind of intellectual history, but readers are on their own in deciding what should be distilled out for the psychological inquiries of today and tomorrow. On a more positive note, what also shines through is the heroic character of a man who always dared to go his own way even when he knew the price he would pay. In the face of a truly anti-human polity, Vygotsky never abandoned the hope of achieving a truly human psychology that encompassed higher mental functions such as consciousness and creativity.

Two major concepts that are pure Vygotskian—"inner speech" and the child's "zone of proximal development"—are dealt with admirably in this book. The discussion of Vygotsky's work with schizophrenic patients and retarded children is succinct and informative.

It would be fascinating to know more of the personal biography of Vygotsky. This book contains an interesting description of his family of origin, his university days, and the poignant moment of his death, but one wants to know more about the man behind the intellect. I wonder, for instance, if there are surviving letters or students' notes that would help bring Vygotsky more vividly to life again. I also would like to know the nature and status of his untranslated writing—my impression is that a great deal of valuable material remains out of reach.

An important historical lesson of this book is that the science of psychology, like other kinds of science, can be influenced in subtle and not so subtle ways by intellectual, philosophical, and political ideologies. This leads Kozulin to ask questions about the priorities and direction of psychological and psychiatric research in the United States. For instance, he questions the reluctance to rigorously tackle the more "human" aspects of mental activity such as creativity and symbolic process. Such questions are worthy of serious consideration.

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CHILD PSYCHIATRY

The Self in Transition: Infancy to Childhood, edited by Dante Cicchetti and Marjorie Beeghly. Chicago, University of Chicago Press, 1991, 383 pp., \$34.95.

This book is the outcome of a conference held at Harvard University in November 1985. It presents research on the self

during the transition from infancy to adulthood. Clinicians may be misled by the title to expect to read about ideas concerning transitional phenomena. Although Winnicott is quoted relatively often, his concepts about the transitional object and its role in emotional development, which would include the progressive integration and differentiation of the self, are not emphasized. Rather, this scholarly volume examines the "interactions among biological, psychological, and sociological factors and of conducting assessments of functioning that span multiple domains."

Some of the authors, especially Stechler, focus on the psychoanalytic model and review current theoretical revisions, such as the abandonment of drive theory, and their relevance to our concepts of the development of the self. For the clinician, these are the most relevant sections because they have many implications about psychopathology as it is understood in terms of defects in psychic structure rather than predominantly in terms of intrapsychic conflict. The self or, as many psychoanalysts would say, the self-representation is a central core of the mental network and undergoes specific vicissitudes in the genesis of psychopathology as a structure and as a response to psychic trauma. It is clinically relevant no matter how it is defined, either as a central core or a supraordinate organization that embodies all aspects of psychic structure and interactions.

The editors begin by giving an excellent overview of the papers that follow as well as stressing the importance of the task they have set themselves. The editors and the authors do not limit themselves to clinical issues. Many of them come from a broad academic tradition, and this is expressed in their writings. Most of the chapters are straightforward and clearly written, but some are weighty and pedantic and tend to be burdensome rather than enlightening. Fortunately, they are in the minority, and I confess this assessment may, in part, be due to my bias. I prefer a clinically oriented conceptual system that has relevance to the treatment process. To me, the examination of psychic structures such as the self is most rewarding when it is placed in a clinical context. Perhaps this is generally true of clinicians' reactions.

I cannot discuss all of the chapters in this book because of space. I will briefly touch on some of the topics to give the reader the flavor of the book. The first two chapters after the introduction are psychoanalytically oriented. Stechler believes that the mode of resolving conflict becomes part of the self. This would indicate that adaptive and defensive patterns as they are consolidated in the ego's executive system contribute to the structure of the self-representation. This includes successful as well as unsuccessful adaptations and places the self in an operational perspective. Emde and Buchsbaum stress that the development of the self moves in the direction of autonomy and that this occurs in the context of connectedness, which means object relatedness. Other authors focus on cultural factors, the effects of social phenomena, and the linguistic approach in the development of the self.

This book covers many diverse topics reflecting the special interests of the behavioral scientists who are the authors. Some of the chapters will be more meaningful than others depending on the reader's orientation. The book ends on a seriocomic note that should capture the interest of most of us. Kagan presents a fictionalized dialogue between an older and younger philosopher, often witty and humorous, which recaps the difficulties involved in the study of the self.

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The Psychoanalytic Study of the Child, vol. 45, edited by Albert J. Solnit, M.D., Peter B. Neubauer, M.D., Samuel Abrams, M.D., and A. Scott Dowling, M.D. New Haven, Conn., Yale University Press, 1990, 546 pp., \$55.00.

The Psychoanalytic Study of the Child has been one of the few central and essential journals of psychoanalysis since its first volume was published in 1945. Founded and managed at first by Anna Freud, Heinz Hartmann, and Ernst Kris, its editorial board and contributors were from the start outstanding psychoanalysts, many of whom made regular and particularly important contributions in its pages.

The last of its 12 original editors died last year, but its tradition and contributors have remained strong under subsequent editors, through three publishers, and through an era of markedly diminished power and influence of psychoanalysis over the past 20 years. The major excitement and centrality of the first 20 or so volumes are no longer there, and some articles in some recent volumes have seemed to be coasting, adding little. However, brilliant and important articles are still there, and in annual volume after annual volume high levels of clinical intelligence, seriousness, complexity, and integration are nearly always still there.

Let me state an interest, lest it be considered a blinding bias: I had a close family and family-friend connection to the editors and many of the contributors for the first few decades of *The Psychoanalytic Study of the Child*; I still have some friendships and friendly acquaintanceships with several current editors and contributors.

Volume 45 has 26 chapters grouped into seven areas: Psychoanalytic Theory, Development, Clinical Contributions, Transference and Countertransference, Self-Esteem and Shame, Termination of Analysis, and Applied Analysis. Child and adolescent issues are prominent, but the volume is not, nor has *The Psychoanalytic Study of the Child* ever been, just about children. Most of the authors are American, plus several Britons and Israelis. Striking to anyone used to reading current psychiatric journals, at least half a dozen carefully detailed case histories are presented and discussed in this volume; one gets the sense of several complex troubled people being well understood and treated over time (see, for example, the chapters by Gavshon, Cohen, Harrison, Ablon, Kaufman, and Lax).

One also gets the sense that even in this decade in which psychiatry often celebrates brain far more than mind, and despite notorious problems with verifiability of analytic hypotheses, psychoanalytic theory is still alive and growing. Gender, ego ideal, entitlement, object relations, attachment and separateness, fantasy, somatization, self-esteem, shame, termination—all receive worthwhile theoretical contributions in the present volume. Anton Kris's chapter, "The Analyst's Stance and the Method of Free Association," is, with its own careful scientific clinical stance, a model of wise theory building.

The chapters in the Self-Esteem and Shame section add to a currently overdue and lively area of exploration, but one might wish some firmer editorial hand had shaped the sprawling chapter by Yorke et al.; the brief chapter by Abrams that follows might, in an ideal world, have been built into, and helped shorten, the previous chapter.

In the section on Termination of Analysis, Jack Novick continues his clear work and adds a provocative potential bridge from child toward adult analysis.

There is a chapter on *The Secret Garden*; a somewhat self-preoccupied chapter on *The Velveteen Rabbit*; a good idea not

wholly shaped and carried out about Alain-Fournier and *Le Grand Meaulnes*; and a chapter by Lenore Terr on Virginia Woolf. I read with pleasure anything that Dr. Terr writes, but (despite its witty title) I found her discussion of Woolf less careful and persuasive than her brilliant earlier work on Poe, Magritte, Hitchcock, Bergman, and King.

One cannot fairly summarize 26 chapters in a brief review, but I can say that although I approached reading volume 45 of *The Psychoanalytic Study of the Child* as a duty, it soon felt like a rekindling of opportunity. I felt energized by reading this volume.

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Psychosocial Issues in Day Care, edited by Shahla S. Chehrizi, M.D. Washington, D.C., American Psychiatric Press, 1990, 285 pp., \$38.00.

The 16 chapters in this volume are grouped under five headings: Developmental Considerations and Day Care, The Relationship Between Parents and Child Care Providers, Pediatric Issues in Day Care, Child Abuse and Day Care, and National Policy and Day Care. The individual chapters are written by clinicians and researchers with substantial experience in their respective fields. The breadth of the approach adopted by the editor makes this a valuable book, especially for those not immersed in day care issues, because it illustrates very clearly how complex many of the issues are, ranging from national social policy to concerns about the individual child, parent, and day care provider.

Zigler and Freedman, in the opening chapter, document the crisis in child care in the United States, including the lack of a national public policy based on developmentally sound practices and the high cost of good quality day care, which in many communities is not available at any price. The harm done to the development of infants and young children who are in day care of poor quality appears clear. There are excellent brief descriptions of current types of day care and a plan for developmentally sound practice. Zigler and Freedman believe that, in spite of their magnitude, the problems are not insoluble. The importance of a parental leave policy as an alternative to infant day care is outlined. The authors also advocate that the "school of the 21st century" be created as a return to the concept of the school serving as a local center for all the social services required by the community, including day care, and note that a number of demonstration schools are now in operation.

Carollee Howes summarizes current research on early child care, and Jay Belsky analyzes developmental risks associated with infant day care. Howes's clear presentation of research issues is particularly helpful to readers not familiar with the field. Three aspects of child care that emerge from child development research as important in facilitating optimal development are especially congenial with the views of the readers of this journal: 1) the stability of the child care arrangement, 2) the quality of the child care, and 3) the interaction between family characteristics and child care. The discussion of the multidimensional influences of early child care on the development of children recognizes the need for research acknowledging such complexity. Belsky's concern about the effect of infant day care on child development includes a review of the research evidence bearing on the issue. He concludes that "extensive nonparental care initiated in the first year is, to a sta-

tistically significant extent, probabilistically associated with insecure attachment, aggression and noncompliance. What remains strikingly unclear at present are the reasons why the associations discerned . . . [in his extensive and thoughtful review of infant day care studies] emerge so persistently in the research literature" (p. 60).

In chapters 4 and 5, Alicia Lieberman and Steven Frankel discuss clinical perspectives in infant day care. Lieberman's sensitive discussion of the subjective experience of the young child in day care suggests that consideration of a competence-based model of infant development versus an anxiety-based model should be of special interest to clinicians. Her integration of these two models illustrates an approach to understanding and improving child care and emphasizes the importance of the clinician as an ally of child and parent in helping them to cope adaptively with the stresses of day care. Frankel underscores the rudimentary status of our knowledge of the long-term effects of day care on the individual. He cites the need for more longitudinal studies and points out that the strength and potential contributions of psychoanalysis in the study of the child's inner world are limited currently by the weakness of its research methods.

Chehrazi calls attention to the experience of parents who must balance working and parenting. Her report of a pilot study in which 20 working mothers were interviewed is followed by a discussion of areas for future research, including part-time versus full-time employment for the mother and the role of the father. Practical suggestions about how to evaluate the quality of child care are included.

Phillips and Whitebook focus on child care providers, beginning with a strong plea for medical and mental health professionals to establish working relationships with day care providers to provide better services for the children who come into health settings. The bulk of this chapter is an excellent and disturbing summary of the multiple factors that work against adequate compensation for child care providers. The authors discuss the compelling need for affordable, high-quality child care, raise concerns about the consequences for children of low standards of care, and present some examples of efforts at solutions.

Patricia Nachman approaches the important role in the lives of young children of child care providers other than their parents. She reports a comparison study in a nursery school setting of extensive observations of two groups of children—one group with their mothers, the other with familiar, constant nonparent caregivers. Nachman examines the roles of the different caretakers in the separation-individuation process and shares her thinking in a stimulating, interesting way.

Barbara Kalmanson's discussion of children's responses to separation focuses on understanding the individual child. She cautions that group data on separation, although providing valuable information, leave many unanswered questions for parents considering day care options for their children. This chapter presents a very useful summary of how parents and day care providers can evaluate the nature, pattern, and magnitude of the child's separation distress, some determinants of the capacity to manage the separation experience, and how parents and day care providers can assist the child.

Pediatric issues in day care are presented by Susan Aronson and Evelyn Oremland. Aronson notes that the United States lacks a surveillance system for infectious diseases and injuries in child care, resulting in a scarcity of data on the health status of children in such settings. She discusses injury control, prevention and management of infectious diseases, and health promotion. Under each topic she summarizes the data avail-

able and discusses corrective action. In addition to the preventive and corrective measures that apply to children's health in general, there is a focus on individual health needs and on the importance of integrating health with other concerns in child care. Oremland's emphasis is on the greater psychological vulnerability of children during illness and the dilemma for parents of deciding when and for how long it is necessary to stay home with their child. Several models for the care of sick children are described. The importance of caregivers' understanding the effect of illness on behavior and the child's need for added support are noted, and helpful, practical suggestions are made.

Robert Kelly's chapter on sexual abuse in day care discusses some of what is known about the reality of sexual abuse in day care in terms of how much and what types of sexual abuse actually occur; the impact on communities, families, and the victims themselves; and how best to cope with the negative impact of sexual abuse. This condensed report of studies and recommendations emphasizes both the impact of sexual abuse and the responsibilities of parents, professional counselors, and the judicial system.

Martin Glasser's chapter on prevention of physical and sexual abuse in day care discusses guidelines for evaluating a prospective center as well as recommendations for prevention and treatment. Clinical vignettes illustrate his major points. He calls attention to variations in a child's experience of trauma related to age, previous history, circumstances of the discovery, and how it is handled by parents, professionals, and the legal system. This is followed by a chapter by Catherine Ayoub, Penelope Grace, and Carolyn Newberger on working with maltreated children and families in day care settings. Emotional abuse and child neglect are discussed, as well as physical and sexual abuse. Here the focus is on how day care programs can alleviate the effects of maltreatment through sensitive, skillful responses to child and family. Thus, day care holds promise as a growth-promoting, therapeutic environment.

In the final chapters, national policy and day care are addressed by Congressman George Miller (D., California), who writes on the expanding federal role in child care, and Carol Stevenson, who discusses child care law and child care advocacy. Miller describes past and current major efforts and some of the major obstacles in the way of developing the child care services so desperately needed. He notes that a policy framework, set in place in the 1980s, requires the backing of fiscal resources, well-trained and compensated child care personnel, and a flexible but firm regulatory structure that ensures safe and nurturing child care environments in every state. Stevenson raises a number of important issues regarding the achievement of a comprehensive system of child care, among them how child care will be regulated; the parents' role; the role of federal, state, and municipal governments; and who will pay and how. The importance of advocates understanding the hard work of finding answers to the questions involved is a central theme.

In summary, Chehrazi has put together a very informative, useful book by a broad array of authors with impressive expertise. Inevitably, there is repetition, but this is no disadvantage, because each chapter can stand alone and the reader is free to choose those topics which address his or her particular interest.

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Attention-Deficit Hyperactivity Disorder: A Handbook for Diagnosis and Treatment, by Russell A. Barkley. New York, Guilford Press, 1990, 747 pp., \$50.00.

Since Barkley's first edition of this book in 1981 (1), much has changed in the diagnosis and treatment of attention-deficit hyperactivity disorder. There has been a flurry of research, changes in diagnostic criteria and philosophies, and the emergence of public awareness about the disorder. This new edition does more than merely update the classic handbook of 1981. It is an entirely new book covering more topics and addressing new issues, not the least of which is that the disorder is different from the one originally described.

The book is divided into three major sections: Nature and Diagnosis, Assessment, and Treatment. The first three chapters provide a historical overview, an elaboration of the epidemiology and phenomenology of attention-deficit hyperactivity disorder, and a review of the conditions that are often comorbid with the disorder. Barkley describes the disorder as a developmental, motivational (not attentional) deficiency with a physiological base and asserts that the inability to adequately regulate behavior by rules and consequences is the hallmark of the disorder. This conceptualization is clearly presented as Barkley's perspective rather than as undisputable fact, a discrimination that is not as easy to make in other sections of the book.

Chapter 4 discusses the developmental course and outcome of children with attention-deficit hyperactivity disorder and the factors that influence prognosis. Chapter 5 describes the parent-child interactions of children with attention-deficit hyperactivity disorder and the psychiatric family histories of these children's biological relatives. Barkley proposes his model for explaining how aggressive behavior develops and is maintained in children with attention-deficit hyperactivity disorder; maternal depression, marital discord, and negative parenting behaviors play major roles. Chapter 6 reviews the diagnostic criteria for attention-deficit hyperactivity disorder as well as for common comorbid disorders. Barkley offers sound advice on supplementing the *DSM-III-R* criteria for attention-deficit hyperactivity disorder with additional criteria to enhance diagnostic specificity (e.g., using cutoff scores from standardized teacher and parent rating scales and lengthening the symptom duration requirement). Barkley's descriptions help the clinician to differentiate the likely etiology and developmental progression of attention-deficit hyperactivity disorder from the other disruptive behavior disorders and from undifferentiated attention-deficit disorder. However, he minimizes the comorbidity of attention-deficit hyperactivity disorder and internalizing disorders on the basis of his own research, in spite of the fact that several of the case histories provided indicate clinically significant elevations in these domains. Given the increasing amount of work on this, one detects a bit of attention deficit in the area. On the other hand, Barkley's discussion of the diagnostic complexities of children who have co-occurring odd thinking, behavior, and affect with seeming attention-deficit hyperactivity disorder is excellent.

The second major section of the book deals with assessment of attention-deficit hyperactivity disorder and begins in chapter 7 with an overview of the biopsychosocial and developmental factors that should be considered in clinical evaluations. Chapter 8 provides a useful "how to" guide on what information should be collected when interviewing the parent, the child, and the teacher. The parent section is supplemented by an interview schedule Barkley developed, which is quite practical and adoptable. A separate section is focused on the

pediatric medical examination, including the medical interview, physical examination, and laboratory tests.

Chapter 9 is an outstanding chapter that explains the role that behavior rating scales should play in the assessment of attention-deficit hyperactivity disorder, provides useful information on the most widely used scales, and recommends particular scales for different types of evaluations. The rating scales are outlined in a highly accessible format that highlights information such as the number of items, factors assessed, availability of reliability, validity, and normative data and where to obtain them.

Chapter 10 provides a brief review of the laboratory measures, neuropsychological tests, and direct observation procedures that have been used to assess children with attention-deficit hyperactivity disorder, discusses their potential clinical utility, and ends with a cautionary assessment of their limitations. Chapter 11 illustrates how to integrate the diverse sources of information obtained in the assessment by presenting six actual clinical cases seen at Barkley's attention-deficit hyperactivity disorder clinic.

Part three of the book addresses treatments of attention-deficit hyperactivity disorder and covers all of the contemporary interventions for the disorder. Many of the chapters are authored or co-authored by colleagues of Barkley's who have developed and implemented programs of their own. Many of the chapters present session-by-session guides on how to conduct the therapy program. These include Barkley's program for counseling and training parents, family systems approaches to parent training (including a family therapy program for adolescents with attention-deficit hyperactivity disorder), behavioral and cognitive-behavioral interventions for the classroom, social skills programs for children with attention-deficit hyperactivity disorder, and assessment and treatment guidelines for adults with the disorder.

Chapter 17 covers medication therapy, and although it is not intended to be a comprehensive or critical review, it presents a clinically useful account of methylphenidate and amphetamine. Controversies (e.g., use of stimulants to treat children with attention-deficit hyperactivity disorder who also have tic disorders) and the practical use of other medications are not covered in the kind of detail that characterizes the other descriptions of treatment.

This second edition of *Attention-Deficit Hyperactivity Disorder* is truly the handbook on the diagnosis and treatment of attention-deficit hyperactivity disorder in the 1990s. It is a readable mix of research findings, personal observations, and clinical implications. Clinicians can find a wealth of useful information that can help them to sharpen their diagnostic skills in identifying attention-deficit hyperactivity disorder, recognize possible comorbid disorders, and broaden their treatment armamentarium. It is a book that addresses a diversity of professionals—psychiatrists, psychologists, pediatricians, social workers, teachers, and school administrators—promoting understanding and hence communication between the disciplines likely to be involved in treating a child or adolescent with attention-deficit hyperactivity disorder. For the practitioner who is likely to evaluate and/or treat individuals with this disorder, it is truly a book worth reading and owning.

REFERENCE

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Childhood Stress, edited by L. Eugene Arnold. New York, John Wiley & Sons, 1990, 573 pp., \$59.95.

Childhood Stress continues the excellent tradition of Wiley's series in child and adolescent mental health. The series presents views on child rearing and child management, child development, child advocacy, and child psychiatry. *Childhood Stress* adds "the most complete and timely coverage" of the major stressors among children and adolescents. Organized into four major sections, the book includes an impressive array of experts who present research findings describing biological aspects of stress, interactions of developmental age with stress, public health aspects of stress (i.e., stressful effects of family and community violence and illness), and assessment-intervention techniques.

I have developed a list of "essential" topics derived from child therapy journals. Arnold covers all but three of these topics and presents additional topics not on my list. Two of the missing topics, childhood stress resulting from living with a terminally ill parent or sibling and stress associated with being the child of a mentally retarded parent, a parent with borderline personality disorder, or a substance-abusing parent, are addressed indirectly. However, given the prevalence of these problems, a more thorough review would have been desirable. Two of the leading stressors for school-aged boys, learning disabilities and hyperactivity, were inadequately addressed.

The references cited come from many fields, with psychiatry predominating. Unfortunately, data from controlled trials are rarely given, and referenced statements are often overgeneralized. For example, no outcome data are presented comparing the effectiveness of different treatments.

Overall, Arnold gives excellent descriptions of childhood stress and meets the goals established for the book and for the series. The copious references will appeal to adventurous readers desiring additional detail. This clearly written book belongs in the library of any professional who is seriously interested in the evaluation, treatment, or management of children. It serves as an excellent reference for the casual reader and a knowledge base for the expert reader.

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PSYCHOANALYSIS AND PSYCHOTHERAPY

The XYZ of Psychoanalysis: Epilogue to a Great Beginning, by Harold Feldman. New York, Praeger, 1991, 192 pp., \$39.95.

Dr. Feldman attributes the recent decline in the appeal of psychoanalysis to the rise of narcissism. To establish his thesis he traces the development of psychoanalysis from its hopeful beginning, when the delineation of the role of the unconscious in symptoms promised to solve the mystery of mental illness, to the current situation of resistance to psychoanalytic treatment. Dr. Feldman compares the course of psychoanalysis to that of Marxism, to which he is also partial. Although Marxism and psychoanalysis differ markedly regarding their concepts of the genesis of human problems, they both have faith that man's rationality can solve both his economic and his psychological problems.

Freud was impressed by the impact of unconscious irrational thoughts and beliefs. He hypothesized that if irrational

unconscious thoughts and beliefs could be subjected to conscious rational consideration through the intervention of psychoanalysis, psychopathology would disappear. Sadly, this did not happen; in spite of the analyst's awareness of some issues, symptoms persisted. As a result of continued observation and study in an effort to gain greater understanding of psychic processes, Freud conceptualized the phenomena of transferences, identification, the ego, superego, and narcissism.

Freud's delineation of the origin of the libido involved in these phenomena is murky. Sometimes he designates the id as the reservoir of libido; at other times he points to the ego. Consideration of the ego adumbrated the phenomenon of narcissism, which according to Dr. Feldman focuses on aggression and destructiveness rather than sexual matters. Dr. Feldman distinguishes between primary and secondary narcissism. Primary narcissists are incapable of relating to objects; thus, transference is not established and psychoanalysis cannot proceed, the relationship to the analyst is archaic, patients do not separate themselves from the analyst, and they expect immediate gratification. The psychic structure of secondary narcissists is more mature, but they manifest some primitive narcissistic issues that make treatment difficult.

The focus of individual psychoanalysis on the importance of gratification has fostered narcissism. The narcissistic position has been reinforced by a society in which technical, economic, and political forces favor its development. Individual pleasure is valued over concern for others. In this atmosphere sociopathy, drug abuse, promiscuity, and irresponsibility flourish. Treatment is sought because of displeasure associated with narcissistic deprivation rather than because of conflict engendered by the thoughts or actuality of gratification.

Although Dr. Feldman faults psychoanalysis for encouraging narcissism, he also extols its capacity to counter it. He believes that psychoanalysis can release the uniting, bonding forces of eros which counter the destructive, restrictive forces of thanatos and set humans free to enjoy a richer, fuller, and cooperative life. He parallels this hopeful prediction for the outcome of the psychological distress of individuals with a satisfying outcome for the problems of society when socialism prevails, as he believes it will. Dr. Feldman's conclusions are appealing but not convincing because the evidence on which they are based is limited and the reasoning reductionistic.

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Interpretation and Interaction: Psychoanalysis or Psychotherapy? by Jerome D. Oremland. Hillsdale, N.J., Analytic Press, 1991, 184 pp., \$29.95.

For quite some time now there has been no more important task in the continually expanding field of the psychological therapies than to render our theories of treatment more precisely. Oremland is right on the mark when he notes that the contemporary therapist carries a legacy of "dissatisfaction and disillusionment that inevitably . . . [followed] the nonspecific application of nonspecific theories to overwhelming problems. It is little wonder that the Golden Age of psychoanalysis [after World War II] was to dissolve into the interactive excesses and emphasis on spontaneity, intuition, and absence of training that [has come to] characterize the scene" (p. 5). The formula with which, in Freud's words, we must alloy the "pure gold of psychoanalysis . . . with the copper of . . . suggestion" has yet to be specified, and the complexities of

that task remain daunting. Oremland's contribution to the discussion is to elaborate on the emerging realization that suggestion is embedded in the very heart and fabric of our work. When Freud wrote of the copper of suggestion he was referring to hypnosis, and we continue to think of suggestion in terms of direct and deliberate uses of authority. But the more astute view is that suggestion is ubiquitously laced into all facets of the therapeutic process, sometimes in ways that are quite obvious, more often with exquisite subtlety. This view compels us to restate Freud's metaphor: there is no pure gold of analysis without infusions of copper. Psychoanalysis is distinguished from its derivative psychodynamic therapies only by variations in the proportion of analytic interpretation to interactive suggestion, and the implications of this revision are a good deal more far-reaching than is at first apparent.

Oremland approaches the problem with these central assumptions: 1) All aspects of psychotherapy are interactive, and all interactions create versions of the therapist within the patient. This often affords the patient substantial palliation without understanding. Oremland quotes Ferenczi: "Suggestion [or interaction] . . . is an education in blindness." 2) The single value embedded within the psychoanalytic orientation is that it is better to know than not to know. 3) Interpretation is an interaction, but it is qualitatively different from other interactions in that its aim is solely to add explicit knowledge. 4) Transference interpretations minimize the suggestive effects of the interpretive interaction by making the interaction itself the object of analysis.

So armed, Oremland delineates a triad of the forms of psychotherapy that are informed by psychoanalytic theory: psychoanalysis, psychoanalytically oriented psychotherapy, and interactive psychotherapy. The first two of these therapies are closely similar because each holds that interpretation of all interactional components of the treatment is the central and distinguishing mode of the therapeutic process. This ambitious and exacting emphasis is designed to minimize the effects of suggestion and to vault understanding. It is an enactment of the assumption that better (palliation without understanding) is inevitably the enemy of best (change based on insight). In both psychoanalysis and psychoanalytically oriented psychotherapy the therapist must be ever mindful to identify and resist the ubiquitous pressures from within and without to treat the patient with transferences. Oremland avers that when the latter happens the therapist has sold the patient short or allowed the patient to sell himself or herself short—that is, to be deprived of the opportunity to achieve personality changes of the greatest possible depth, scope, and stability.

There are differences between psychoanalysis and psychoanalytically oriented psychotherapy, but those differences are small in comparison with the extent to which both differ from interactive psychotherapy. In the former the goal is to reduce the suggestive effects of interaction to a minimum by assiduous attention to transference analysis. The opposite is true in interactive therapy. Here the therapist deliberately intensifies aspects of the therapeutic interaction in order to achieve specific goals. Thus, interpretations and other interventions are used as overt and covert directives and suggestions. In interactive psychotherapy, interpretations of the transference are counterproductive insofar as they undermine the intended effect of indirect interactive directives.

Oremland works his way through the major aspects of the psychoanalytic theory of treatment in order to present his clarifications of basic concepts and use them to explicate the distinctions between the different forms of psychotherapy. His clinical examples are rich and clear, and they touch on a raft

of important technical issues and points of theory often misunderstood. For example, neutrality is neither emotional involvement of the therapist nor an affectation of nonresponsiveness. It is the assiduous attempt to keep the field of interaction as undistorted as possible in order to direct the patient's attention to hidden meanings of his or her words and actions in the therapy. In the same vein, on the supposed antithesis of support versus insight in psychotherapy, Oremland says that interpretation is the most supportive of interventions because it adds comprehension to that which is being experienced. Conversely, interactive therapy, not psychoanalysis, is most regressive in its effects on the patient because it engenders unresolved dependency and thus fails to extend the purview of personal responsibility.

If psychoanalytically oriented psychotherapy and psychoanalysis both rely on interpretation as their central mode, how do they differ? The external differences have mostly to do with training of the therapist (analysts are more rigorously trained), the range of patients treated by the method (psychoanalytically oriented psychotherapy applies more broadly), frequency of sessions, and use of the couch (Oremland argues that the use of the couch in psychoanalytically oriented psychotherapy is counterproductive). The essential difference is none of these but lies, rather, in the dominant area of interplay. In psychoanalytically oriented psychotherapy the actualities of the psychotherapeutic interaction—the here-and-now—take precedence, whereas in psychoanalysis the internal soliloquy of the analysand is intensified so that the historical aspects of life experience predominate. However, "in both, a past is located that enriches the present. In both, the future is determined by achieving a fuller, multidimensional understanding of the present" (p. 119). Oremland goes to great lengths to be fair in his comparative evaluation of the different therapies. He allows that psychoanalysis and psychoanalytically oriented psychotherapy are so similar that ultimately there may prove to be little difference between them. But he doubts it, even as he admits that the superiority of psychoanalysis is unproven. Ultimately the question of efficacy "must . . . be considered in the context of the imprecision that colors indications and goals for all the psychotherapies" (p. 122). From the sole vantage point of symptom alleviation, interactive psychotherapy is probably the most widely effective form of treatment, except that in choosing this course the therapist forgoes the promise of the benefits of insight.

Oremland acknowledges his debt to Merton Gill for his own work, for his careful reading of the manuscript that became this book, and then for his acceptance of the offer to write a concluding response, which has been included in the book as a final chapter. In this chapter Gill brings his own seminal thinking to bear on what Oremland has written. In all the major areas they agree, but it is Gill's manner to hone his incisiveness on issues of difference. He leans away from Oremland's triad of therapies toward the idea of a continuum that admixes the balance of the dose and effects of interaction and interpretation. He is less sanguine than Oremland on the question of how far interpretation can be relied on to reduce the interactive effects of interpretation. Gill notes that one cannot *always* interpret the transference and that it is dangerous to believe otherwise because excessive emphasis on transference interpretation is an interaction of major dimensions. In the main, however, Gill lauds Oremland's text and highlights its accomplishments.

Oremland is known through his writing and teaching for his wide range of psychoanalytic scholarship. However, the discoveries about interaction that led to this book appear to have been derived from his own astute clinical observations

rather than his reading of Sullivan or Kohut or the British object relations theorists. He has breached the classical psychoanalytic model of mind as an internally regulated closed system, but he leaves it to Gill to propose that his ideas represent the context of a new paradigm: "It would be an error to read Oremland's monograph as a brief for the employment of the usual analytic technique but at a lesser frequency and sitting up. His major thesis is, rather, that with the recognition of the social nature of the analytic situation the issues of the ubiquity of interaction and the distinction between interaction with and without the analysis of the interaction become central" (p. 142). "The application . . . of these ideas requires a thoroughgoing acceptance of the reality and ubiquity of the interpersonal and interactive nature of the therapeutic situation . . . It also requires a willingness to accept the fact that either we enter into an affective relationship with our patients or we defend ourselves against it. We have no other choice" (p. 161). These truths certainly are not new, but they have been afforded scant attention in the practice and theory of psychoanalysis and its derivative therapies in the United States. That deficiency is in the process of being corrected, and in no small measure the credit goes to thinkers like Oremland and original works such as this one.

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The Use of the Self: Countertransference and Communication in the Analytic Situation, by Theodore J. Jacobs. Madison, Conn., International Universities Press, 1991, 238 pp., \$27.50.

It is not infrequent that a book with a title referring to psychoanalytic psychiatry is relegated to analytic institutes or the back shelves of science libraries. Theodore Jacobs' most recent book, however, is one that I hope will not suffer the same fate. In it are many ideas and concepts that are of use to psychiatrists who do psychotherapy of all types and are applicable to an audience of general psychiatrists as well.

Much of the book consists of Jacobs' reflections on his experiences with patients in analysis. These are used as clinical illustrations of aspects of transference and countertransference discussed in the book. In an interesting twist of parallel processing, Jacobs' willingness to write about his personal reactions to patients and to share his own experiences invites the reader to reflect on his or her own interactions with patients. This self-disclosing and interactional style of writing serves to convey one of the main concepts in the book. Reading, like psychotherapy, is transformed into an interpersonal phenomenon. The reader/psychotherapist is influenced by the communication of the writer/patient rather than simply acting as an objective and nonparticipant observer. The evocation of thoughts and memories from the reader as a result of Jacobs' own self-disclosure mirrors the manner in which we are influenced during the course of our interactions with patients.

A corollary to the interpersonal nature of therapy is that transference phenomena must develop in the context of the patient-therapist interpersonal relationship. Rather than the "traditional" view of transference as a purely intrapsychic phenomenon, Jacobs reconceptualizes transference as a product of each unique patient-therapist combination, in which each member of the dyad contributes important past and present experiences and associations. The therapist's ability to understand his or her own contributions to this dynamic re-

lationship is paramount in fostering the emergence of a more complete understanding of the patient. Jacobs argues quite convincingly that awareness of all aspects of patient-therapist communication, particularly nonverbal communication, is essential to furthering understanding. According to Jacobs' model, therapists' recognition and awareness of such things as their own physiological responses and mental imagery during sessions can be used to facilitate an understanding of the patient.

In later chapters, Jacobs describes some ways in which therapists can collude with patients in concealing important information or emotions. This often results from therapists' resistance to examining their countertransference responses and ultimately hinders the conduct of psychoanalysis. One could well make the case that resistances to recognizing countertransference responses to patients hinder the delivery of therapy of any kind. In extreme cases, a therapist's ignorance about his or her contributions to the therapeutic relationship can lead to repression of emotional reactions on the part of the therapist that are nonetheless evident to the patient. These become secrets shared by the patient and therapist. To illustrate this point, Jacobs describes a case in which one of his patients discovered some information about a painful personal loss Jacobs had recently experienced. Through several sessions, Jacobs ignored the patient's hints about the possession of this knowledge. It was only after coming to what Jacobs describes as a personal understanding of his own grief reaction that he was able to hear these messages from his patient and to analyze the ways in which these secretive communications from the patient had been reflected in the therapeutic relationship.

It is unfortunate that Jacobs' book is aimed at such a narrow audience. The ability to understand our responses to patients and to attend to all forms of communication between ourselves and our patients are skills that should be developed in all psychiatrists. Although the examples used by Jacobs are from analytic cases, they are nevertheless applicable to all professionals who interact with patients. An understanding of our limitations and very human reactions to patients and the way they ultimately affect our interactions with patients would be well advised in all practitioners of medicine, particularly when the profession is being taken to task for its lack of empathy. This book should serve as a reminder to both clinician/readers and mentor/authors—to clinicians who would do well to broaden their understanding of themselves and their patients and to mentors who would do well to encourage us to do so.

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Conflict and Compromise: Therapeutic Implications, edited by Scott Dowling. Madison, Conn., International Universities Press, 1991, 248 pp., \$32.50.

This is a curious book, one that begins to make any kind of sense only after reading the entire text and getting the gist of its political agenda. It starts off, incomprehensibly, with three theoretical papers that have nothing to add to what has been known for years now among orthodox psychoanalytic theorists. It is difficult to understand why this monograph in the Workshop Series of the American Psychoanalytic Association should begin with a set of stale theories. We are told, for example, that "the history of the patient's neurotic conflicts is

reenacted in" the analytic setting, as if no one has ever challenged the idea that psychoanalysis succeeds in becoming in reality a laboratory-like situation. Numerous modern workers have pointed out the multiple tilts introduced by so-called classical analysis in the relationship that develops between therapist and patient.

When clinical issues are raised in the first three chapters, they are barren of reports of sensitivity on the part of therapists to the role of their countertransference reactions toward patients. There is one illustration of a clarinet-playing patient that is designed to illustrate the concept of sublimation, but it reads like a travesty of Freudian thinking dating from before World War I; the author reduces the musical accomplishment to a series of sexual conflicts without an adequate awareness that human achievements defy such belittling.

Chapters 4, 5, and 6 deal with case material, and they are as interesting as all reports of clinical encounters are bound to be. As with the early chapters, however, I felt increasingly uneasy about a lack of adequate material about what was most idiosyncratic about the therapists themselves, except perhaps that they felt secure in safely practicing a well-established science without need of any special justification.

The remaining half of the book is made up of "discussions," starting off with a piece by Charles Brenner, a leading orthodox psychoanalytic theoretician. After a second, unilluminating chapter, there follow two chapters that help explain, I think, the purpose of *Conflict and Compromise*. Here we find a section written by a Kleinian analyst and then a piece composed by a self psychologist. Notice that these appear in the "discussions" rather than in chapters equal to those which begin the book. I found the self psychology chapter potentially arresting, but it looks like it will be another generation until a Jungian gets allowed into the fold at such orthodox "workshops." One of the early theorists in the text tells us that "numerous psychoanalytic contributors have carefully built up this new knowledge during the past fifty years without much fanfare or polemic insistence on forming new schools" without seeming to be aware how smug such a sentiment sounds.

Once the Kleinian and the Kohutian have had their say, the book concludes with the responses of the original authors. I found a tone of weary superiority over innovative ideas, combined with self-congratulation about what has already been accomplished. The Kleinian and the Kohutian are very well behaved, and there is no sound here of the thunder of battle, or even the life of the mind.

Psychoanalysis cannot survive, I think, without a great deal more openness. *Conflict and Compromise* does not read like a workshop where people are genuinely testing out new ideas or groping for new formulations. Parts of it sound like a funeral dirge; and if the point of the exercise was to demonstrate so-called toleration toward a Kleinian and a Kohutian, then I think that the illusion of genuine debate can do damage in reinforcing the prejudices and preconceptions of the old establishment.

A sound book might have given substantial conceptual standing to viewpoints other than the ones expressed in the bulk of the text. As it is, *Conflict and Compromise* will not change the way anyone thinks, although it may get added (surely unread) to the bookshelves of orthodox psychoanalysts.

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PSYCHIATRIC PRACTICE

Confidentiality Versus the Duty to Protect: Foreseeable Harm in the Practice of Psychiatry, edited by James C. Beck, M.D., Ph.D. Washington, D.C.; American Psychiatric Press, 1990, 212 pp., \$25.00.

In the past 20 years the number of reporting duties imposed on psychiatrists has increased dramatically. In the past, exceptions to confidentiality were mandated primarily for the benefit of the patient. A therapist's duty was essentially only to the patient. Within general medicine, physicians were required to report patients with epilepsy who operate vehicles, patients with gunshot or knife wounds, and those with contagious diseases. These exceptions had few effects on the practice of psychiatry.

Today, psychiatrists are obliged to report or otherwise protect against danger posed by their patients. Along with other physicians, they are obliged to report abuse of children and the elderly, and, as a condition of payment for their services, they must report information to third-party payers.

Since the well-publicized case of *Tarasoff* (1), there have been more than 70 published cases in which psychiatrists and other psychotherapists as well as hospitals and other health care facilities have been named as defendants in suits alleging breach of the duty to warn or protect. Troubled by the prospect of liability, state psychiatric societies have pushed for legislation spelling out clearly their duty under the law and restricting the duty to a warning. Legislation to this effect has been adopted in a number of states.

The specter of AIDS-related *Tarasoff* suits now worries many psychiatrists. Sexual partners of individuals with AIDS are foreseeably endangered. Does this create a legal duty for the psychotherapist of an AIDS patient and, if so, how does the therapist fulfill it?

In dealing with children and families, therapists are confronted with child abuse reporting laws. How do therapists treat a pedophile when they are obliged to report? How do they treat a parent who abuses a child when they are obliged to report?

How do therapists treat patients with antisocial personality disorder when, by definition, they pose a problem to society? The difficulty in protecting third parties from the violence of an antisocial patient is complicated by the fact that one of the standard ways of carrying out an assumed duty to protect potential victims is to attempt civil commitment, but in most jurisdictions, a person who is not actually harming someone does not fit the statutory definition of mental illness.

The past decade has witnessed greater public attention to the hazards arising out of the use of motor vehicles. Alcohol or drug use has compounded the danger. Some state statutes require that physicians report patients with conditions that may affect their ability to drive. Some cases, modeled on the *Tarasoff* decision, speak to an obligation to protect the public that is not based on statute.

Sexual activity between therapists and patients has attracted increasing attention. Three states have enacted statutes requiring a therapist to report a former therapist accused by a patient of sexual exploitation to the appropriate licensing authority or to inform and enable the patient to report.

This book covers these and other issues. Dr. Beck opens the book with two overview chapters, followed by Robert I. Simon's chapter on the duty to protect in private practice, Kimberly White and Beck's on the duty to protect in emergency psychiatry, Bruce Gage's on the duty to protect in inpatient

psychiatry, Richard Barnum's on managing risk and confidentiality in clinical encounters with children and families, Spencer Eth and Gregory B. Leong's on therapist sexual misconduct, Kenneth Appelbaum and Paul S. Appelbaum's on the patient with HIV, Stephen J. Bartels and Robert E. Drake's on the dual-diagnosis patient, Landy F. Sparr and David J. Drummond's on posttraumatic stress disorder and the duty to protect, Joseph B. Layde's on the antisocial patient, and Sally L. Godard and Joseph D. Bloom's on driving, mental illness, and the duty to protect.

Eth and Leong suggest cautioning patients that the therapeutic relationship is not sacrosanct, thus conveying the essence of a *Miranda*-like warning. Simon suggests documentation on the assessment of violence.

The value of warnings remains to be proven. In *Tarasoff*, when the therapist notified the police, the patient left treatment and subsequently carried out his threat. In Detroit, when the police are informed that a patient poses a danger, the usual response is, "We're busy with dead bodies. We can't be bothered with threats."

Haunted by fear of a lawsuit, therapists lose the ability to think clearly and to rely on their clinical judgment. This book may prove helpful, but good clinical judgment remains the best guide for the clinician. In most circumstances, the actions the therapist may take to protect others are the same actions that will be of clinical benefit to the patient. As a basic principle, it will almost always be in the patient's interest to be prevented from harming other people. In any event, the odds of a psychiatrist being sued for breach of the duty to protect, going to trial, and being found liable are 5,800 to 1 in any one year.

The book reads easily, has little overlap, reflecting good editing, but lacks an index.

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DISEASES OF THE ELDERLY

Subcortical Dementia, edited by Jeffrey L. Cummings. New York, Oxford University Press, 1990, 267 pp., \$45.00.

For a new disease to be recognized, its signs, symptoms, and course must be distinguished from traditional formulations of similar presenting conditions. Such is the case made by the authors of this book for subcortical dementia, a syndrome of cognitive dysfunction characterized by defective recall, poor abstraction, and loss of initiative and associated most commonly with changes in mood and motor behavior as well. Aphasias, apraxias, or agnosias are generally absent, in contrast to cortical dementia. Despite strong support from recent research elaborating cognitive functions of the striatum, the concept of subcortical dementia is not without controversy. What purpose is served creating yet another, somewhat artificial dichotomy? Is it legitimate or useful to describe subcortical dementias as reversible and cortical syndrome as irreversible? Most dementing diseases and lesions involve circuits having both cortical and subcortical components, making as-

essment of the relative contributions of each anatomical area problematic.

This book is the first coordinated response to such concerns, written by true believers who present a scholarly defense of the history of subcortical dementia, its neurochemistry and anatomy, and its characteristic profile in Huntington's and Parkinson's diseases, progressive supranuclear palsy, multiple sclerosis, and AIDS dementia complex. Of greatest interest to psychiatrists are two chapters masterfully integrating neuropsychological and physiological changes in depression and in normal aging from a subcortical perspective. Notably absent, however, is a chapter that summarizes the literature on tardive dysmetria and the adverse cognitive sequelae of long-term neuroleptic use, a topic seemingly quite germane to subcortical dysfunction. Clinical and management implications of the diagnosis of subcortical dementia are in general subordinated to more theoretical and phenomenologic observations.

As might be expected from a syndrome still being defined, tautologies and contradictions emerge. Aphasia, excluded by most authors, is put forth as a central feature in a chapter reviewing focal subcortical lesions. In contrast to patients with Huntington's disease, patients with Korsakoff's disease are described at one point in the book as benefiting from procedures that increase the opportunity for encoding, while in another chapter and table, encoding enrichment is viewed as unhelpful in cortical and beneficial in subcortical dementia. The concept of perseveration is also variously defined. The methodology of studies unsupportive of the dichotomy is often critiqued but positive reports are embraced without comparable scrutiny. Most of the studies reviewed on cognitive change in AIDS dementia fail to control for adverse effects of medication or concomitant depression, and few of the reports comparing cortical and subcortical dementias account for possible differences in severity, stage of illness, or treatment differences. However, in academia, as in football, the best defense is a good offense, and these authors move down the field convincingly. The writing is concise, the graphics are of high quality, and the book is well referenced and edited. There is joy, too, in encountering an idea still so fresh that its complete history and literature can be definitively examined in a 267-page book.

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Family Involvement in Treatment of the Frail Elderly, edited by Marion Zucker Goldstein, M.D. Washington, D.C., American Psychiatric Press, 1989, 240 pp., \$28.50.

This book is number nine in the Clinical Practice Series of the American Psychiatric Press, which, according to series editor Judith Gold, attempts to "provide current, factual, and theoretical material of interest to the clinician working outside of a hospital setting" (p. xi). Unfortunately, this promise is not fulfilled.

In her introduction, Dr. Goldstein defines the frail elderly as "those who cannot live or travel independently, cannot maintain interest in self and others, and require a so-called 'therapeutic environment' in the community or institutional setting" (p. xv).

She goes on to note that "an effort has been made to leave it up to the practitioner/teacher to translate into practical use the theoretical and informative material presented in this volume" (p. xvii).

Chapter 1, "Parent Care," by the editor, is the most interesting in the book, principally because of Dr. Goldstein's gripping account of her attempts to deal with her demented mother, first in a "personal care home," and later in a skilled nursing facility. As the baby boom population ages, one in three families in the United States will have a frail elderly member to care for.

In chapter 2, "Spouses as Caregivers: Stresses and Interventions," Steven Zarit, Richard Birkel, and Eileen Malonebeach inform us that 36% of all caregivers are spouses (23% wives and 13% husbands). We learn what caregivers must cope with, including activities of daily living (helping the patient bathe, toilet, and dress), "positive" symptoms (wandering, agitation, and forgetfulness manifesting itself in the interminable repetition of questions), and "negative" symptoms (the amount of time needed for household and family activities formerly performed by the patient). We learn the mediators of care demands (the family's financial resources, amount of substitute caregiving, and amount of emotional support available) and the problems associated with caregiving (decreased physical and emotional well-being, financial problems, and social isolation).

The empirical findings on caregiving by spouses are slender. One finding is that spouses are more reluctant than children to institutionalize a patient with dementia. Using a behavioral model, the authors briefly discuss interventions such as providing the family with information about the disease, helping develop more effective management strategies, arranging substitute caregiving, and recommending legal and financial counseling.

In chapter 3 Kenneth Sakauye deals with "Ethnic Variations in Family Support of the Frail Elderly." Once again, there is little empirical research to draw on. Approximately 10% of the population over 65 is nonwhite. Multi-infarct dementia is the major cause of dementia in blacks and Asians, whereas Alzheimer's disease is the major cause in whites. The onset of chronic illness and disability frequently occurs at a younger age in nonwhites, but suicide rates and rates of institutionalization are lower in nonwhites.

In chapter 4, "Mutual Support Groups for Families of Alzheimer's Disease Patients," Martha Bell recommends self-help support groups as effective vehicles to assist families. She discusses guidelines for the formation of a support group, including frequency (once a month on a weekday evening), length (two hours), those most likely to attend (primary caretakers or an adult child), and possible leaders. She provides a 28-page appendix listing the local chapters of the Alzheimer's Disease Association and the state commissions on aging.

Chapter 5, "Economic Supports for Family Caregivers of the Elderly," by David Beigel et al., consists largely of the results of a survey of state units on aging. Once again there is a state by state listing of the meager supports available, including tax credits and deductions and direct payment programs.

In the final chapter, "Medical Students' Attitudes Toward the Care of the Frail Elderly and Their Families," Leah Dickstein et al. note that clinicians are prejudiced against the elderly, seeing them as more emotionally ill, inactive, dependent, and socially undesirable. This chapter is mostly devoted to the results of a study in which medical students completed a questionnaire before and after their psychiatry clerkship. The results demonstrated that the students' attitudes to the elderly became more positive after the clerkship.

This book will be of interest to psychiatrists preparing for the geriatric psychiatry examination. The information it pre-

sents is insufficiently detailed to be of much practical use to the psychiatric clinician in helping families manage their frail elderly.

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AIDS

Behavioral Aspects of AIDS, edited by David G. Ostrow. New York, Plenum, 1990, 430 pp., \$55.00.

When the institutes of the Alcohol, Drug Abuse, and Mental Health Administration first announced plans to fund research studies about HIV infection and AIDS, many critics argued that the money would be wasted. Give the money to the virologists and immunologists, they argued, and soon we will know everything about what causes AIDS, how to treat HIV infection, and how to make a vaccine.

The AIDS epidemic is now 10 years old. An enormous amount has been learned about the virus that causes the disease, but sadly our treatment efforts are mostly palliative and, at least at this writing, we do not yet have a vaccine. Zidovudine is the only drug specifically developed and marketed to treat HIV so far, and it clearly does not cure HIV infection. The most successful medical interventions for people infected with HIV have been drugs that control the secondary, opportunistic infections. Most of these, like pentamidine for the treatment of pneumocystis pneumonia, were discovered before the outbreak of HIV.

At this time, the only way to prevent HIV infection is behavioral change; therefore, the research that has gone into understanding how that can be accomplished is absolutely critical in fighting HIV infection. This book, consequently, contains some of the most important information a scientist, clinician, or concerned citizen interested in HIV infection and AIDS could possibly read.

This book is encyclopedic. It is organized into four main sections. First is a section called AIDS: Contributions of the Behavioral Sciences; this section includes discussions of psychiatric and psychological aspects of AIDS and other sexually transmitted diseases. The second section is Prevention: HIV Risk Reduction. The third is Neuropsychiatric Aspects of AIDS, and the fourth is Health Care Delivery Issues.

The book has many strengths. It is so comprehensive that most readers will want to pick and choose among chapters. Except for the omission of the basic science of retroviral infection of nervous tissue, it is hard to think of any topic related to behavioral and CNS aspects of AIDS that is not here. The chapters deal sensitively with the particular needs and issues of gay people, minorities, and women. They often paint a dramatic and moving picture of life with AIDS for both victims and caregivers. And they contain information of diverse kinds, from the results of brain imaging studies to lists of organizations in U.S. cities that provide help for patients.

The book begins with a beautifully written chapter by Daniel Defert called "A New Social Reformer: The Patient." Defert shows great compassion for health care workers who must change fundamental attitudes because of the epidemic and convinces us that patients with AIDS will reform medical practice worldwide. Robb W. Johnson, David G. Ostrow, and Jill Joseph provide a comprehensive review of "Educational Strategies for Prevention of Sexual Transmission of HIV" and remind us that merely knowing how AIDS is transmitted is

entirely inadequate for fostering change of high-risk behavior. The authors note, "Education that aims solely to increase knowledge would appear to be limited in its ability to induce and maintain alterations in behavior" (p. 45).

One of the most compelling chapters is by Ritch C. Savin-Williams and Rand E. Lenhart. Titled "AIDS Prevention Among Gay and Lesbian Youth," the chapter is outstanding in its sensitivity and clear recommendations for better treatment of gay youngsters. The chapter is full of information on the psychosocial development of gay and lesbian youth and offers practical guidelines for health care personnel who interact with them. A chapter by Dooley Worth on "Women at High Risk of HIV Infection" is well written and highlights how much more we need to know about the specific problems and characteristics of women with AIDS. Also commendable are chapters on "Intravenous Drug Use and AIDS," "Diagnosis and Treatment of Neurologic Disorders in AIDS and Other Sexually Transmitted Diseases," "HIV Disease: Brain-Behavior Relationships," and "Adjuvant Treatment of HIV Dementia With Psychostimulants."

The book is not perfect, of course. Too many of the authors rely on anecdote and personal observation, and references are often to obscure, nonrefereed journals. A chapter on management of neuropsychiatric disorders in HIV-positive patients states that "anxiety disorders are especially prevalent . . . mood disorders can include major depression, suicide, and affective psychoses" (p. 174). The reference for this is a general review, leaving the reader wondering if there are any data to support these claims. In fact, recent experimental evidence suggests that psychiatric disorders may be no more common among patients with HIV infection than in the general population.

A chapter on diagnosis and treatment of acute psychological problems in HIV-infected patients persistently insists that panic attacks occur in HIV infection, although again there are data against this. This chapter also claims that "the additional propensity of some antidepressants to induce leukopenia must also be borne in mind" (p. 199), again without presenting any evidence for a side effect of antidepressants with which I am

not familiar. The statement in another chapter that "in our experience, neurologic deficits and psychiatric symptoms usually coexist" (p. 272) is interesting but, once again, unsupported by experimental evidence. A chapter on "Mental Health Services Delivery Issues" by James J. Strain and George Fulop contains very interesting information on instruments for assessment of cognitive function in patients but also takes annoying and gratuitous shots at *DSM-III-R* that are irrelevant and should have been edited out.

There are the usual problems with redundancy. Half a dozen chapters review the fact that HIV infects the CNS and causes neuropsychiatric complications. There is also a lack of careful editing, with a few too many grammatical errors and misspellings; these fine authors deserved better from the publisher.

But all of these are relatively minor quibbles. The way to correct the few problems in this excellent book is obvious. Dr. Ostrow should be urged to begin a second edition immediately. This could include some of the data on prevalence of psychiatric disorders in HIV infection and on the use of psychoactive medications in patients with AIDS that became available after the book went to press.

While we wait for the second edition, there is plenty to be informed and moved by in this first edition. Ostrow, J. Hampton Atkinson III, and Igor Grant note that "in the early days of AIDS and treatment, psychiatrists, psychologists, and other mental health caregivers came on the scene mostly as an afterthought, providing support or understanding to victims of a catastrophic illness or to manage the occasional behavioral or neuropsychiatric complications. The studies reviewed here and our ongoing work indicate a true primary role of psychiatry in the diagnosis and treatment of these patients" (p. 183). For those interested in accepting that primary role, this book is a very good place to start.

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Reprints of Book Forum reviews are not available.

Letters to the Editor

Addition of Fluoxetine to Clozapine

SIR: Fluoxetine has been added to typical neuroleptics for treatment-resistant symptoms in schizophrenia (1, 2). We report a case of adding fluoxetine to clozapine for a schizophrenic patient with obsessive symptoms. The only other reported concomitant use of neuroleptics and fluoxetine involved a nonschizophrenic patient who had a grand mal seizure while taking clozapine, clomipramine, and 100 mg/day or more of fluoxetine (3).

Mr. A was a 39-year-old man with a diagnosis of chronic paranoid schizophrenia beginning at age 20 when he felt people were talking about him. Symptoms of agitation, persecutory delusions, and thought broadcasting led to several hospitalizations. Auditory hallucinations, "people talking together," became prominent 10 years after onset. Past treatments included trials of chlorpromazine, fluphenazine, and haloperidol; imipramine and trazodone were tried adjunctively; and a course of ECT had been given. Although improving from exacerbations of his symptoms, he continued to have persecutory suspiciousness, ideas of reference, social withdrawal, and anxiety.

Mr. A was placed on clozapine, and his dosage gradually increased to 800 mg/day. Over the next year he showed improvement in symptoms but continued to be anxious, misinterpreted talking and laughing as directed at himself, and mainly complained of repetitive cursing thoughts. While not a complaint before, cursing thoughts had occurred earlier during a drug withdrawal exacerbation. This symptom was experienced as an intrusive and unwanted product of his own mind, and he fought it with repetitive, idiosyncratic prayers and by trying to think opposite thoughts. The obsessive quality of this symptom led us to consider a trial of fluoxetine, which was started at 20 mg every other day and increased over 5 months to 80 mg/day. A reduction to 60 mg/day was necessary due to tremor and nervousness.

Within the first 4 months, episodes of intrusive cursing thoughts were reduced in frequency and intensity. Mr. A found it easier to suppress these thoughts when they started. Eye contact and rapport with staff improved and anxiety was lessened. He also felt a subjective improvement in mood and energy. Referential ideation occurred intermittently but less frequently, and he continued to have anxiety interacting with strangers. The patient noted how his mind had cleared. Family and nonstaff health professionals remarked on Mr. A's improvement.

Adding fluoxetine to clozapine in the treatment of schizophrenia may be potentially useful. Fluoxetine may raise clozapine levels, as seen with haloperidol (4), and aid improvement. However, fluoxetine may potentiate akathisia and extrapyramidal side effects (5), absent with clozapine, resulting in treatment failure. The potential antagonism between a serotonin (5-HT) reuptake inhibitor and a 5-HT₂ receptor blocker presented no clinical dilemma.

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Polyserositis Associated With Clozapine Treatment

SIR: Recently there has been much written concerning the side effects of clozapine (1-3). Polyserositis associated with clozapine therapy has not been reported in the literature. We present a patient who developed both pleural and pericardial effusions during a trial of clozapine. The effusions resolved when the drug was withdrawn and developed again when clozapine treatment was restarted. Our experience with this patient suggests that polyserositis may be a complication of clozapine therapy.

Ms. A was a 39-year-old woman with a diagnosis of chronic schizophrenia. She had a traumatic brain injury at age 16 and a subsequent grand mal seizure disorder. She had no prior history of respiratory or rheumatological disease. She had been treated over 17 years for auditory hallucinations and disorganized behaviors with chlorpromazine and fluphenazine hydrochloride with some limited success but developed significant extrapyramidal side effects. She was therefore hospitalized for a supervised trial of clozapine. An initial dose of 25 mg/day was increased by 25 mg every other day. On day 9 of treatment, at a dose of 150 mg/day, she developed a temperature of 101.4 °F (rectal) without any sign of infection. It was believed that the elevated temperature was secondary to a drug fever associated with clozapine. On day 16, at a dose of 350 mg/day, the patient continued to have intermittent temperature elevations to 102 °F (rectal), and a chest X-ray revealed bilateral pleural effusions, greater on the left than the right. Clozapine was discontinued at this time. Analysis of the pleural fluid revealed an exudate (protein=3.0 g/dl, LDH=614 IU/liter) with no organisms identified on gram stain, acid fast stain, and aerobic and anaerobic cultures. The pleural fluid cell block showed numerous neutrophils and reactive mesothelial cells. The patient was reactive to an anergy panel but nonreactive to purified protein derivative. HIV testing was

negative, and amylase was not elevated. A rheumatologic work-up, which included antinuclear antibodies, erythrocyte sedimentation rate, and rheumatoid factors, was non-diagnostic. A repeat chest X-ray 9 days after discontinuation of clozapine treatment revealed complete resolution of the pleural effusions. At this time clozapine treatment was restarted at a dose of 25 mg/day and increased 25 mg per day.

On day 6 of the second clozapine trial the patient again developed an elevated temperature to 102.4 °F (rectal), and chest X-ray revealed recurrence of the left pleural effusion. Clozapine was discontinued at this time, and within 7 days radiologic exam showed the pleural effusion had resolved. An echocardiogram at the time of the recurrence of the pleural effusion showed a moderate pericardial effusion with no compromise of cardiac function. A repeat echocardiogram 2 weeks after the discontinuation of clozapine revealed complete resolution of the pericardial effusion.

Ms. A was also taking valproic acid and fluoxetine during the clozapine trial. The patient had been taking both of these medications for several years without any adverse effects. She continued taking these medications throughout the trial and after the clozapine was discontinued and the pleural and pericardial effusions resolved. Given these facts, it is unlikely that either of these medications, alone or together, caused the effusions.

A pharmaceutical corporation has previously received the following reports of adverse reactions associated with clozapine: one case of polyserositis, one case of pleural effusion, and separate cases of pericardial effusion and pleural effusion, both with associated pericarditis. In all cases a direct link to clozapine could not be established but in each case the effusions resolved with discontinuation of the clozapine (personal communication).

Although we are unable to say with certainty that the pleural and pericardial effusions were a direct result of clozapine therapy, the lack of evidence of other etiologies, the temporal relationship of the development and resolution of the effusions with the initiation and discontinuation of clozapine, and previously reported cases to the drug manufacturer suggest this medication was the cause of polyserositis in our patient.

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Disulfiram Toxicity and Catatonia in a Forensic Outpatient

SIR: Although disulfiram has been widely used by patients without detriment to their physical or mental health, incidents of disulfiram toxicity have been extensively reported in the literature (1). It is also well documented that catatonic behavior can and does occur without the presence of psychoses (2).

Several earlier single case studies have linked the occurrence of nonpsychotic catatonic behavior to disulfiram toxicity (3). It appears that certain individuals may be predisposed to suffer disulfiram-induced catatonic symptoms.

We report a case of a forensic outpatient with a major mental illness who was treated with disulfiram in addition to antipsychotic medications. As the duration of disulfiram treatment lengthened, the patient became increasingly catatonic and eventually required hospitalization. It should be noted that the patient had no prior history of catatonic symptoms secondary to his schizophrenic illness.

Mr. A was a 56-year-old man with a history of paranoid schizophrenia and alcohol abuse who was found not guilty by reason of insanity and recently discharged from a state mental hospital. As a condition of release into the community (4), he was ordered by the local superior court to begin a medication regimen of disulfiram, 250 mg daily, in addition to his trifluoperazine, 10 mg/day, and trazodone, 50 mg/day. Approximately 3 weeks after beginning the disulfiram, Mr. A was taken to the emergency room of a local hospital after exhibiting shortness of breath, confusion, memory loss, and disorientation. These symptoms had escalated during a 12-day period following an episode of syncope. The results of an initial CT scan indicated no abnormalities, and the patient was admitted to the neurology ward in the hospital for further testing. He was thought to suffer from some toxic metabolic abnormality. Infectious process and drug screen both proved negative. An EEG indicated moderate, generalized, nonspecific abnormalities. No epileptiform discharges or focal abnormalities were observed, though prominent theta activity was noted. The lumbar puncture produced a clear, colorless fluid. ECG results indicated a normal sinus rhythm.

A psychiatric consultation was obtained. Mr. A was believed to be suffering from delirium with underlying schizophrenia. All psychiatric medications, disulfiram, trifluoperazine, and trazodone, were discontinued. Initially he demonstrated a marked decrease in reactivity to the environment. He sat nearly motionless, and his affect was flat. He was oriented only to person, with memory 0/5 after 5 minutes, and able to follow only simple one-step commands. With the cessation of all medication, he gradually improved. At the time of discharge, 12 days following admission, he was again normally responsive to his environment, alert, communicative, oriented, and able to follow complex commands. He demonstrated no memory impairment and had a full range of affect. He was ambulatory and able to care for himself. It is believed Mr. A suffered from disulfiram toxicity which accounted for the change in his mental status. He resumed trifluoperazine, 5 mg/day, as an outpatient and has been functioning well, without further incidents.

Cases such as this lend support to the argument that catatonia should be considered a separate diagnosis in *DSM-IV* (5), distinct from schizophrenia. Addition of such a diagnosis would alert the physician to the diverse etiologies of catatonia and guard against diagnostic confusion and inappropriate treatment as a symptom or subtype of schizophrenia when it is unrelated to this major mental disorder.

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Protecting Patients From Clinician-Patient Sexual Contact

SIR: A recent court decision, *Bash v Board of Medical Practice* (1), reflects an important, and in our opinion, alarming trend in the current debate as to what is the most appropriate preventive measure to protect patients from the harms that accompany clinician-patient sexual contact. The decision in question affirmed a medical board's decision to require, in the conditions for reinstatement of a psychiatrist found guilty of exploiting the physician-patient relationship for his own sexual gratification, a permanent restriction prohibiting him to treat females.

While such categorical restrictions might be appropriate in other contexts, such as the treatment of patients with pedophilia, they do little to address the underlying failures of self and clinical management that characterize patient-clinician sexual contact.

In our forensic psychiatric experience, as well as in the experience of our colleagues, cases where such contact has occurred are also characterized by other serious breeches of the standard of care, such as the failure to focus on the development of a therapeutic alliance essential for treatment to proceed. Until the offending clinician demonstrates that such failures have been remedied, we are concerned that the clinician who cannot be considered as competent to treat women should be considered as competent to treat men. Moreover, we are concerned that such categorical half-way measures perpetuate the traditional stereotypes of women as "the weaker sex," stereotypes that in themselves have all too often limited the scope of therapeutic efficacy. A professional who subscribes to the stereotype of women as either objects to be exploited or protected is seriously impaired in treating both women and men.

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Major Depression or Alcohol-Induced Organic Affective Syndrome?

SIR: Capt. John R. Cusack's review of William Styron's *Darkness Visible: A Memoir of Madness* (1) included the suggestion that the book "should be requisite in the core curriculum for psychiatric residents." Styron's account of his struggle with depression was also widely acclaimed in the popular press for its artful description of depressive symptoms. While *Darkness Visible* (2) may be compelling reading, critics in gen-

eral and Capt. Cusack in particular have unfortunately not addressed the critical point side-stepped by Styron himself, which is the link between previous alcohol dependence and depression. Styron reported a history of alcohol abuse over 40 years; he abruptly stopped drinking 6 months before his hospitalization at age 60. Styron's formulation does not include the possibility that his alcoholism had engendered his depression; he discounts this possibility ("it had never truly depressed me during my drinking career, acting instead as a shield against anxiety"), proposing that the absence of alcohol made him "emotionally naked, vulnerable [to depression] as I had never been before." He concluded, "I shall never learn what 'caused' my depression, as no one will ever learn about their own."

In fact, recent research has attempted to characterize the specific pattern of depressive illness seen in alcoholics after periods of observed sobriety. Dackis et al. (3) concluded in their study of 49 severely depressed alcoholics evaluated after a period of documented sobriety that, given the atypical pattern of recovery from severe depression, many of the alcoholics probably "did not, in fact, have major depression. Instead they may have had alcohol-induced, organic affective syndromes." Cook et al. (4) studied 58 male inpatients over 55 years old with nonbipolar depression, of whom 16 had a history of alcoholism. Results tentatively supported the concept of subtyping elderly depressed patients in terms of past history of alcoholism. They concluded that "the pattern of their illness tends to be more chronic" compared with depressed elderly men without a history of alcoholism, suggesting an etiologically distinct pattern of depression or the possibility that "alcohol exposure induces organic changes of the central nervous system which persist, and predict poor response to treatment."

If *Darkness Visible* were made requisite reading, as suggested, then consideration of these and other investigations that systematically examine the link between alcoholism and depression should be required as well.

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Capt. Cusack Replies

SIR: Dr. Hersh's comments are appreciated. His remarks blend a book review of a literary work with a clinical case presentation; my review critiqued the book, not Mr. Styron's illness. A review of the latter based on an autobiographical work would be presumptive.

The link between alcohol dependence and depression is well documented, complex, and important. However, the thrust of *Darkness Visible: A Memoir of Madness* is Mr. Styron's illustrative and poignant portrayal of depressive illness.

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Serotonin Function in Depression: Effects of Seasonality?

SIR: Lawrence H. Price, M.D., and colleagues (1) are to be commended for their study of responses to intravenous L-tryptophan (L-Trp) in such a large group of patients (N=126) and comparison subjects (N=58), but several questions are raised by their work. Contrary to previous reports in depressed patients, they reported that the mean peak Δ prolactin response following intravenous L-Trp was significantly *elevated* in melancholic patients (N=68, mean=4.2 ng/ml, SD=2.0) compared to control subjects (mean=3.1 ng/ml, SD=2.0, $p<0.03$). This surprising finding prompted me to review the published reports of prolactin responses to intravenous L-Trp in healthy control subjects (2-6), including all those referenced by the Yale investigators. In the ten studies which used doses of approximately 100 mg/kg (N=134) or 7 g (N=50), the mean peak Δ prolactin for healthy control subjects (of both sexes) ranged from 4.6 to 25.5 ng/ml with a mean of 13.8 ng/ml. This is substantially higher than the mean 3.1 (SD=2.0 ng/ml) reported by Dr. Price and colleagues.

In attempting to account for the variance in the system, the authors appropriately addressed the factors of age, gender, and nutritional status but did not account for a possible seasonal influence. In a study of 16 control subjects and 15 non-depressed bulimic patients, peak Δ prolactin responses following L-Trp, 100 mg/kg i.v., varied significantly by season (6). These data are compatible with other data in humans suggesting a nearly annual rhythm in normal 5-HT function (6). The reported variance attributable to seasonality in these studies is at least as great, if not greater, than that of gender and age. Interassay differences tend to be much lower and are probably not responsible for such variance. It would be a major contribution to the field of psychoneuroendocrinology if Dr. Price and colleagues reanalyzed their data assessing for a seasonal effect, e.g., by using a two-way analysis of variance using season and affective diagnosis as grouping variables in the total group and in each gender.

This brings up a statistical point. The authors decided to \log_{10} -transform their data "because of nonnormal distributions," although a review of mean peak Δ prolactin responses in table 2 of their article indicates little or no difference in the standard deviations for the various diagnostic groups. The parametric requirement for homogeneity of variance appears to have been met and, if so, \log_{10} -transformation is therefore unnecessary. In addition, only two of the other 14 published reports of prolactin responses following L-Trp have been \log_{10} -transformed.

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Dr. Price and Associates Reply

SIR: We thank Dr. Brewerton for his careful reading of our paper. We, too, were surprised by the enhanced prolactin response to intravenous L-Trp in melancholic depressed patients compared to control subjects. As we indicated, this may have reflected artifact (since it was entirely accounted for by differences in baseline plasma tryptophan) or differences in our sample of depressed patients compared to those studied by other investigators.

We were also aware of the lower mean peak Δ prolactin responses for healthy controls in our study relative to those reported by others. However, our baseline prolactin levels in all diagnostic groups were low as well, so that our peak Δ prolactin responses to L-Trp were proportionately similar to those reported in other studies. We carefully reviewed our assay methodology and found no evident reason for our low prolactin levels. We can only surmise that assay differences account for the discrepancy between our average levels and those of other investigators. In any case, all prolactin assays in our study were run using the same kit, so that observed differences between diagnostic groups should still be valid.

Although it is true, as Dr. Brewerton points out, that there was little difference in the standard deviations of the mean peak Δ prolactin responses across diagnostic groups, this does not alter the fact that the neuroendocrine responses were not normally distributed. In previous studies, we and others have surmounted this difficulty by utilizing nonparametric statistics. In the present study, we decided to use more powerful parametric methods in order to examine the effects of a large number of potentially confounding variables. Although our samples were sufficiently large to have perhaps justified the use of parametric statistics on the raw data, we decided to proceed more conservatively by applying the \log_{10} -transformation. Analysis of the untransformed raw data did not alter the major conclusions of the study.

Since submitting this paper, we have become aware of Dr. Brewerton's work on the seasonal variation of neuroendocrine responses to L-Trp. Preliminary analysis of our data appears to confirm a seasonal effect, again without any apparent effect on the major findings of our study. We are continuing our analyses and plan to publish the results when completed.

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GEORGE R. HENINGER, M.D.
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New Name for ECT Could Backfire

SIR: I understand the helpful intent of the authors who have argued for a new name for ECT, but I am concerned that such an effort could backfire (1, 2). It would take a long time, if ever, for the term "ECT" to be replaced by "cerebroversion" or another term. During that transition period, patients might be given information about and consent to "cerebroversion" only

to find out later from a friend, nurse, or other patient that what they in fact had received was "shock treatment." This belated discovery might undermine the patient's confidence and lead the patient to feel "tricked." It is for this reason I usually introduce the term "shock treatment" when discussing ECT with patients. A name change should take into account the additional confusion and suspicion it would generate.

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W. VAUGHN MCCALL, M.D.
Salem, N.C.

Dr. Kellner and Dr. Steele Reply

SIR: Change of any kind is difficult, as Dr. McCall suggests. Even after a less frightening term for ECT is adopted, old habits may persist. The difficult transition from *DSM-II* to *DSM-III* offers ample testimony to the staying power of terms and concepts that many believe have outlived their usefulness.

We think that finding a better name for ECT need be neither deceptive nor defensive. A part of obtaining informed consent, as outlined by one of our previous correspondents (1), can include mention of "shock therapy" as an earlier, albeit outdated, descriptor. We simply suggest that clinging to the phrases "shock" (or "electro" or "convulsive") as hallmarks of a treatment modality brings conceptual baggage that is both outdated and unnecessary. Similarly, we do not believe it is defensive to try to avoid frightening people gratuitously. Ideally, a new term will occupy the middle ground between the excessively graphic and the euphemistic.

Has the profession lost a precious heritage by replacing such terms as Mongolian idiot, moron, mental defective, or constitutional psychopathic inferior? Should psychiatric hospitals still be called insane asylums? Should we call stereotactic radiosurgery "X-ray brain cell incineration"? As we previously mentioned, the imaging technique known as nuclear magnetic resonance was renamed magnetic resonance imaging to avoid the frightening connotations of nuclear energy. This was neither deceptive nor defensive, but rather an effort to avoid needless anxiety. Because the change occurred early in the life of the technology, it aroused little opposition.

Little did we realize, when one of us (C.H.K.) proposed changing the name of ECT, that we were beginning a correspondence that would stretch over the next 2 years. Madison Avenue ignored our subsequent plea to help the field come up with a suitable name, and we are beginning to fear that this effort may be closer to the spirit of Pandora than Diogenes. Nevertheless, we maintain that clinging to the starkest possible words to describe the procedure is in no one's best interest—certainly not that of our patients, who may unrealistically fear one of the safest and most effective treatments in all of medicine.

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Borderline Personality Disorder in Incest Victims

SIR: In the recent article by Elizabeth F. Pribor, M.D., and Stephen H. Dinwiddie, M.D. (1), the authors discussed lifetime prevalence of psychiatric illness in incest victims and comparison subjects. I was very surprised to see that borderline personality disorder was not listed among the diagnoses considered. Borderline personality disorder is well known to be associated with childhood sexual abuse, and it would have been interesting to compare the prevalence of this with other disorders. I wonder if Dr. Pribor and Dr. Dinwiddie would care to comment.

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Dr. Pribor and Dr. Dinwiddie Reply

SIR: We agree with Dr. Karagianis regarding the importance of evaluating borderline personality disorder in adults with a history of childhood sexual abuse. Stone (1), Shearer et al. (2), and Ogata et al. (3), have recently reported on the prevalence of incest in hospitalized inpatients with borderline personality disorder. Brown and Anderson (4) reported an association of borderline personality disorder in those individuals with a history of childhood sexual and/or physical abuse in a large psychiatric inpatient sample. An assessment of the prevalence of borderline personality disorder in outpatient incest survivors would represent an important clinical contribution.

Our study design entailed interviews which were quite lengthy (3 hours on average). While we considered including other evaluations in the interview, including a standardized assessment of borderline personality disorder, time was a prohibitive factor. In addition to antisocial personality disorder on axis II and the axis I diagnoses reported in our article, we collected information about personality characteristics. We are presently examining this data for possible publication.

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ELIZABETH F. PRIBOR, M.D.
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The Treatment of Catatonia: Benzodiazepines or ECT?

SIR: We wish to respond to recent letters in the *Journal* concerning the treatment of catatonia (1-3). In particular we would like to address the contention of Stephen J. Masiar, M.D. (1), and Max Fink, M.D. (2), that ECT ought to be the first line of treatment for patients with this condition. Dr. Masiar refers to the "unique role ECT plays in reversing catatonia" while describing the "psychopharmacologic options" as "quite limited." Dr. Fink goes further, suggesting that physicians confronted with a catatonic patient should be "encouraged . . . to introduce ECT at the earliest opportunity." He supports this recommendation with the assertion that "catatonia is remarkably responsive to ECT" while the efficacy of benzodiazepines in treating this condition is "poorly founded in the literature."

We would suggest that the case for ECT as the treatment of first choice of catatonia is far less convincing than Dr. Masiar and Dr. Fink would have us believe. We are unaware of any published evidence that ECT is superior to sham ECT in treating catatonia and can find no randomized controlled studies demonstrating the superiority of ECT over pharmacotherapy with barbiturates or benzodiazepines. On the contrary, as Jeffrey D. DeLisle, M.D. (3), adroitly notes in his reply to Drs. Masiar and Fink, there is evidence that the barbiturate sodium thiopental, routinely used as anesthesia for patients undergoing ECT, may be just as effective as the convulsive treatments themselves in treating the catatonia.

In comparison with the data involving ECT, the evidence supporting the use of benzodiazepines to treat catatonia is relatively strong. In addition to over 35 case reports that have appeared since 1986, there are two larger series describing the rapid and robust response of catatonia to the benzodiazepine lorazepam (4, 5). In our own continuing study we have used low-dose lorazepam to treat 39 episodes of catatonia in patients admitted to our acute care psychiatric hospital ward. The mean age of these patients was 44.2 years, and the duration of the catatonia prior to treatment ranged from 2 days to 2 weeks. Following administration of 1-2 mg of lorazepam, 33 of the 39 episodes (82%) resolved completely within 3 hours. In two other instances the response was more delayed. High doses of lorazepam have not been required.

As mentioned in our earlier article, there appears to be a tendency for catatonic patients to relapse unless the lorazepam is maintained during the initial treatment of the underlying illness. To date none of the patients studied has gone on to require ECT for their catatonic state.

The advantages of lorazepam over ECT in the treatment of catatonia are as follows:

1. The response to lorazepam is apparent within a matter of hours.
2. Low-dose lorazepam is an extremely safe intervention with minimal side effects.
3. Catatonic patients, by virtue of their mutism, immobility, and withdrawal, are generally unable to give informed consent. Treatment then requires consent from next of kin. In our experience families are far more willing to give consent for medication than for ECT.
4. If a patient responds to an initial dose of lorazepam and becomes cooperative and verbal, it is then possible to do a full interview to determine the underlying psychiatric diagnosis and to assess whether he or she is competent to make decisions regarding further treatment.

We fully recognize that, once the catatonic syndrome has resolved and a full assessment can be made, ECT may prove to be the treatment of choice for the underlying illness for

some patients. What we are disputing is the recommendation that ECT be used as a first-line treatment for the catatonia itself.

We hope these comments might serve to give a more balanced appreciation of the treatment options available for this condition.

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Dr. Masiar Replies

SIR: I appreciate the concern of Dr. Rosebush and associates regarding treatment strategies of catatonia wherein they caution against ECT as a first-line treatment for this disorder. In my initial response to the report by Dr. DeLisle I described a definitive treatment approach for catatonic states which may evolve from a variety of syndromes. Abrams and Taylor (1, 2) have carefully delineated the predominant underlying etiology of catatonia as usually major affective disorder, most often the manic phase of bipolar illness. Clinicians are well aware of the extreme danger manic delirium may represent. As such, I continue to advise early consideration of ECT for these patients, as the usual practice of exhausting all pharmacologic options prior to recommending a clearly safe and effective modality seems unsupportable.

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STEPHEN J. MASIAR, M.D.
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Dr. Fink Replies

SIR: Dr. Rosebush and colleagues are fortunate in their success with lorazepam in relieving symptoms of catatonia. In arguing against the use of ECT as a first-line treatment for catatonia, I believe they are setting up a straw man.

They argue that our suggestion that ECT be considered in the treatment of catatonia, regardless of associated symptomatology or diagnosis, is too encouraging and that the efficacy of ECT in such conditions is unproven. They describe

their success: "Following administration of 1–2 mg of lorazepam, 33 of 39 episodes (82%) resolved completely within 3 hours. In two other instances the response was more delayed." They account for 35 patients. I would enquire as to the fate of the four patients who seemingly failed to respond; did they recover spontaneously or go on to an unfavorable outcome?

I raised the question of ECT in the context of a report by DeLisle (1) of a schizophrenic patient with severe catatonia who temporarily responded to midazolam, but when repeated administrations failed "she began refusing all medication, suffered a partial catatonic relapse and worsening of psychosis, and went on to a prolonged course of illness." We suggested that ECT should have been considered, providing support for this view from the historic literature.

We recently reviewed the hospital records of patients identified as schizophrenic, catatonic type, on their admission or discharge diagnoses between 1985 and 1990 (unpublished, in preparation). We identified 20 patients who had received a wide range of treatments. Ten had received repeated courses of benzodiazepines, mainly lorazepam, without success. Nine of these received ECT; eight responded well and were discharged much improved or recovered. Four were discharged with diagnoses of major depressive disorder, with psychosis and catatonia, and four with diverse organic affective disorders. It was this salutary experience, in the face of failures with benzodiazepines, that led to my comment on the case reported by DeLisle. The course of one of the patients was reported by Fricchione et al. (2).

Fricchione (3) recently reviewed the experience with benzodiazepines in catatonia. He noted many reports of success but cites instances in which these drugs failed. He concluded: "Given the significant morbidity and mortality associated with catatonia, ECT should be considered if an expeditious 48- to 72-hour benzodiazepine trial is unsuccessful." That is our present practice.

It is useful to realize that the syndrome of catatonia is no longer "scarce." It is gratifying that the *DSM-IV Options Book* (4) proposes to recognize catatonia as a modifier of various axis I diagnoses, including affective disorders and organic affective disorders. Such recognition will surely encourage the use of ECT in catatonic patients when a trial of benzodiazepines fails, for it will free practitioners from the limitations inherent in the teaching that ECT is not indicated in patients with schizophrenia.

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MAX FINK, M.D.
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Childhood Factors in Adult Self-Destructive Behavior

SIR: The otherwise excellent article by Bessel A. van der Kolk, M.D., and colleagues (1) on childhood factors in adult

self-destructive behavior contains two misleading statements that are not really supported by their data.

They state, "The earlier the trauma, the more cutting." However, what they found was that trauma from adolescence was related to suicide attempts alone, whereas trauma from early childhood and latency was also related to cutting. Moreover, the findings from early childhood and latency were the same. The analysis should have used age of trauma as a continuous variable to clarify whether it was related to the severity of any particular symptom.

They also state, "Although childhood trauma contributes heavily to the initiation of self-destructive behavior, lack of secure attachments maintains it." However, what the authors found was that neglect correlated with self-destruction at intake and was a more stable predictor of the continuation of self-destructive behavior during the study, which does not necessarily shed light on the origins of such behavior during childhood development. Another plausible explanation is that, since all these patients were in treatment, when these behaviors were related to trauma the patients were more approachable in therapy, while when the behaviors were related to neglect, treatment was less effective.

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Dr. van der Kolk and Associates Reply

SIR: We are somewhat surprised by the complaint in the letter by Dr. Paris and Dr. Frank that the data in our article do not substantiate our statement, "The earlier the trauma, the more cutting." This clearly represents an incorrect reading of our data. As they suggested, we did use age of trauma as a continuous variable to see whether it was related to the severity of any particular symptom. In table 3 of our article we showed that trauma in infancy was related to cutting at the $p < 0.001$ level; trauma during latency at the $p < 0.01$ level. In contrast, there was only a trend in the relationship between trauma in adolescence and cutting. Thus, the relationship between trauma and cutting clearly diminished with age.

Similarly, our data clearly supported our statement that trauma contributes heavily (though not exclusively) to the initiation of self-destructive behavior, while lack of secure attachments maintains it. Trauma was the most important predictor of self-destructive behavior prior to our subjects' entrance into our study. However, after being in the study for an average of 4 years, and usually receiving considerable psychotherapy, it was the subjects with the most severe histories of neglect (and sexual abuse) who continued to engage in self-destructive behavior (see table 4). As we stated in our discussion, the subjects with histories of severe childhood neglect seemed to be at least capable of making use of interpersonal relationships during adulthood to help them stop their self-destructive behavior. We thus agree with the critique's "alternative" explanation that "when these behaviors were related to

trauma the patients were more approachable in therapy, while when the behaviors were related to neglect, treatment was less effective," and stated so in our article.

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JUDITH L. HERMAN, M.D.
Cambridge, Mass.

Antidepressants and the Treatment of Stuttering

SIR: John Paul Brady, M.D. (1), recently reviewed the pharmacology of stuttering. I found this review timely and wide in scope. However, by stating that antidepressants have not been evaluated in the treatment of stuttering, Dr. Brady prompted me to inform you that I (2) treated 19 stutterers with mianserine, 30–60 mg/day, for 3 weeks. Twelve of them had Hamilton and Zung scores in the depressed range. Predominantly clonic stuttering was more frequent among these twelve patients ($p=0.03$, Fisher's exact test) than in the remaining stutterers.

Ten of the stutterers with depressive scores and one without a depressive score responded well to mianserine in terms of their stuttering ($p=0.01$, Fisher's exact test). All stutterers with predominantly clonic dysfluency responded to mianserine. Improvement in Hamilton and Zung scores was significantly correlated with the changes in the number of dysfluencies, except for loud reading. Six stutterers who responded to mianserine reported drowsiness in the first 5 days of treatment.

I agree with Dr. Brady that fluoxetine and clomipramine deserve evaluation in stuttering.

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Dr. Brady Replies

SIR: Dr. Costa's interesting abstract eluded my computer-aided search of the literature. It is one of few efforts to identify a subclass of stutterers who may be selectively responsive to a particular medication. In this study, patients with "clonic" stuttering (i.e., those with a preponderance of repetitions of speech sounds rather than prolonged blocks in the flow of speech) benefited the most from mianserine. This drug is a tetracyclic which strongly inhibits the reuptake of serotonin. It is not available in the United States. Controlled clinical trials of mianserine and other antidepressants with strong serotonin reuptake inhibiting properties (e.g., clomipramine, fluoxetine, fluvoxamine, sertraline) would be interesting. I understand that trials of some of these agents in the treatment of stuttering are in progress.

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Philadelphia, Pa.

Alexithymia and the ECA Study

SIR: Gregory E. Simon, M.D., M.P.H., and Michael Von Korff, Sc.D., (1) have reported interesting data from the National Institute of Mental Health (NIMH) Epidemiologic Catchment Area (ECA) first-wave results regarding the relationship of somatization to psychological or emotional distress and diagnosis. They find that patients with multiple somatic symptoms also report multiple emotional symptoms and frequently meet criteria for psychiatric diagnoses. They go on to conclude that, because subjects with high levels of somatic symptoms also have high levels of psychiatric distress, alexithymia, a construct used to describe people who have difficulty recognizing or discussing emotional issues, should not be extended to somatizing patients. I question this assertion.

The original descriptions of alexithymia were rooted in clinical material from patients who demonstrated difficulty discussing their emotional states, had a paucity of fantasy life, and had a concrete, reality-based pattern of communication (2–5). As originally described, often these patients could identify a feeling or affective state but had difficulty amplifying upon this verbally. For example, a patient might be able to say "I am angry," but be unable to elaborate how he or she was aware of this anger or what thoughts or fantasies preceded or accompanied this feeling. The structure of the NIMH Diagnostic Interview Schedule (DIS), the instrument used to assess symptoms, does not require respondents to identify, discuss, or expand upon any particular symptom. Rather, they merely have to endorse it in a yes or no format.

Alexithymic patients may very well be able to do this, yet be unaware of the depth or significance of the feeling which they have endorsed. The measuring of alexithymia has been problematic, and I suggest caution in "rating" alexithymia based upon the number of items positively endorsed from a checklist. Furthermore, prevailing views have blurred the distinction between "psychosomatic disorders" and other disorders that have both somatic and psychic components, making the distinction between psychosomatic disorders and somatizing patients less clear.

Another concern with the interpretation of the data stems from the well-known tendency toward co-occurrence which has been shown in the NIMH ECA data (6). It may be that subjects who endorsed symptoms of psychiatric distress also endorsed symptoms of somatic distress, thus making it likely that if they had a psychiatric disorder, they would likely show many somatic symptoms as well. Again, concluding "that masked psychiatric morbidity among the high somatization group was atypical" fails to take this into account and discounts the meaning and attribution of symptoms which is quite germane to the concept of masked symptoms.

I believe that the authors importantly point out the high co-occurrence between psychiatric and somatic symptoms. However, alternate explanations for this need to be considered before firm conclusions can be drawn.

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Dr. Simon and Dr. VonKorff Reply

SIR: We agree with Dr. Lesser that an epidemiologic assessment such as the DIS cannot provide the same understanding as a clinical assessment. Consequently, our results do not argue against the existence or importance of alexithymia in any individual patient. In the community sample we described, however, functional somatic symptoms did not typically function as defenses against awareness of psychological distress. "Somatizers" were aware of and quite willing to report anxiety and depression.

We also agree that the distinction between psychosomatic disorders and somatization remains unclear, but we hope that our findings might sharpen it. Descriptions of alexithymic patients with classic psychosomatic diseases (hypertension, peptic ulcer) emphasize the physical consequences of denying or avoiding psychologic distress. Somatizing patients, however, usually display an increased sensitivity to all types of distress, both physical and psychological. The two groups might be regarded as lying on opposite ends of a spectrum of symptom sensitivity.

Many multisymptom patients freely acknowledge that their physical symptoms and emotional distress are intertwined. Medical and mental health providers, however, may focus on or give credence to only one domain. Effective, patient-centered care will require providers and patients to integrate the physical (e.g., pain or fatigue), emotional (e.g., depressed mood or anxiety), and behavioral (e.g., reduced activity or social withdrawal) components of illness.

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Antidepressant-Induced Mania in Obsessive-Compulsive Disorder

SIR: Warren Steiner, M.D., C.M. (1), has recently reported a case of fluoxetine-induced mania in a patient with obsessive-compulsive disorder. The author's patient presented a good response to 20 mg/day of fluoxetine with regard to her obsessive-compulsive disorder but soon developed a hypomanic syndrome and her dose of fluoxetine had to be lowered. This led to the recurrence of obsessions and compulsions, but a subsequent increase to the initial fluoxetine dose plus addition of clonazepam, 0.5 mg/day, finally succeeded in keeping the patient asymptomatic of both mood and obsessive features. The author concludes that all patients treated with fluoxetine, regardless of primary psychiatric diagnosis, should be monitored for the development of mania.

A more significant finding, nevertheless, involves the fact that Dr. Steiner's patient finally remained euthymic and free of obsessive-compulsive symptoms. Antidepressant-induced

mania in obsessive-compulsive patients has already been reported elsewhere (2, 3), but both reports stated the impossibility of keeping the patient euthymic without the recurrence of obsessive-compulsive disorder. We recently reported a case of recurrent clomipramine-induced mania in a patient with obsessive-compulsive disorder (4). Neither lowering clomipramine dose nor adding lithium carbonate or neuroleptics succeeded in keeping the patient asymptomatic of both mood and obsessive features. Interestingly, obsessive-compulsive symptoms remitted during the manic episode but reemerged insidiously as soon as the manic syndrome responded to treatment and/or clomipramine was lowered. During the past 3 months this patient was treated with fluoxetine, but while she did not become manic again, her severe obsessions and compulsions unfortunately were refractory to even high doses of this drug.

An inverse relationship has been postulated between obsessive-compulsive disorder and mania (3). Indeed, primary mania is an extremely rare complication of obsessive-compulsive disorder. We have suggested that abnormal regulation of brain serotonergic function might be related to at least some aspects of this supposed pathophysiological relationship (4). Since fluoxetine, a selective serotonergic antidepressant, clearly induced mania as long as obsessive symptoms improved in Dr. Steiner's patient, we might consider this hypothesis further supported. However, since that patient finally reached euthymia free of obsessive-compulsive symptoms, one might speculate that some other mechanisms and neurotransmitters should be involved. Despite its high potency inhibiting serotonin reuptake, clomipramine also has noradrenergic properties, which should be considered with regard to the previous case reports on this issue. Such cases as Dr. Steiner's illustrate that the role of antidepressants inducing mania in several types of psychiatric patients deserves further research.

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Dr. Steiner Replies

SIR: Dr. Vieta and Dr. Bernardo raise the interesting question of the relationship between mania and obsessive-compulsive disorder and of the pharmacological basis of the manic switchover in these patients. It is likely that the switchover processes in obsessive-compulsive disorder patients and in patients with mood disorders are different, as various antidepressants seem to present a different risk of development of mania when used in patients with obsessive-compulsive disorder or mood disorder. In obsessive-compulsive disorder pa-

tients treated with fluvoxamine, Jefferson et al. (1) found a 25% switchover, while in mood disorder patients treated with fluvoxamine a 0.6% incidence has been reported (2), indicating that patients that with obsessive-compulsive disorder may be at greater risk of developing mania. However, with other serotonin-specific reuptake blockers this dramatically increased rise for obsessive-compulsive disorder patients has not been found. Sertraline, which has been found to be ineffective in treatment of obsessive-compulsive disorder (3), has not as yet been reported to precipitate manic episodes in patients with obsessive-compulsive disorder. This lower risk of a manic switch with a medication that is ineffective in treating obsessive-compulsive disorder may in fact support the hypothesis of an inverse relationship between obsessive-compulsive disorder and mania. This relationship could also be explained by the greater selectivity for serotonin reuptake blockade compared to noradrenaline reuptake blockade found with sertraline when compared to other serotonin specific reuptake blockers (4). It is possible that a certain minimum blockade of noradrenaline reuptake is essential for treatment of obsessive-compulsive disorder as well as for the development of mania in these patients. An interesting report of the use of metergoline in reversing clomipramine-induced improvement in obsessive-compulsive disorder symptoms (5) leads one to wonder whether serotonin antagonists could also reverse antidepressant-induced mania in obsessive-compulsive disorder patients who switchover. If so, this would certainly support the hypothesis of an inverse relationship between mania and obsessive-compulsive disorder.

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WARREN STEINER, M.D.
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Obsessive-Compulsive Disorder in Relation to Body Dysmorphic Disorder

SIR: We read with interest the recent article on body dysmorphic disorder by Katherine A. Phillips, M.D. (1). Dr. Phillips suggested that body dysmorphic disorder is related to obsessive-compulsive disorder, and that dynamic factors are also involved. We recently evaluated a patient who appeared to meet criteria for both obsessive-compulsive disorder and body dysmorphic disorder.

Ms. A was a 17 year old who presented complaining of compulsive skin picking and feared disfigurement. The pa-

tient had been experiencing intrusive and distressing images of "pus" under her skin pores for 4 years. She began to pick her skin at a mirror, using a pin to get the "pus" out. She had no concern over her skin's natural appearance, realizing no one else could see the alleged problem. Nonetheless, she was unable to pass a mirror without picking her face, shoulders, back, and breasts, ultimately causing some skin changes. She would spend a half hour in the shower to undo the damage. She was unable to stop her behavior.

Six months of dynamic psychotherapy failed to relieve her symptoms. Ms. A achieved considerable insight into her symptoms. The patient's mother, a university anthropologist, had impressed upon the patient the diversity of beauty in various cultures. However, clear skin, her mother stressed, was valued throughout the world. Following this discussion, the patient experienced the intrusive images. In therapy, the patient learned how conflicted and ambivalent her relationship was with a perfectionist and controlling mother who focused on skin. Also a perfectionist, the patient became even more distressed with imagined damage she was doing to her skin.

Mental status evaluation revealed a young woman with very mild acne. She showed obvious embarrassment at her symptoms but was not able to control her compulsive skin picking. Her Yale-Brown Obsessive Compulsive Scale score was 24; Beck Depression Inventory score was 9. The patient and her parents requested behavioral therapy.

Jenike (2) suggested that compulsive face picking is a relatively rare disorder seen primarily in young women with mild acne, responding to treatments useful in obsessive-compulsive disorder. Our patient did not limit the picking to just her face but appeared otherwise similar to Jenike's patients. Our patient met full criteria for both obsessive-compulsive disorder and body dysmorphic disorder. Other reports stress that body dysmorphic disorder may respond to serotonergic antidepressants useful in obsessive-compulsive disorder (3). As Thomas (4) suggested, body dysmorphic disorder may be primary or secondary, and in our patient it appeared to be secondary to a primary obsessive-compulsive disorder. It is possible that character traits, obsessiveness and perfectionism, would predispose this patient to both disorders.

From a dynamic perspective, Ms. A's mother was dominant, perfectionist, and focused on skin. The patient attempted unsuccessfully to neutralize anxiety around her conflict with her mother through repression and displacement. Intrusive images were the symptom of this conflict, not imagined ugliness. Anxiety was defended against through classic doing and undoing. The behavior resulted in minor skin changes, about which the patient became phobic and avoidant.

We thank Dr. Phillips for her cogent discussion of the complex interrelationship between body dysmorphic disorder and obsessive-compulsive disorder. We hope our case has been helpful and illustrative.

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Dr. Phillips and Dr. McElroy Reply

SIR: We read the letter by Dr. Tanquary and associates with great interest, as it raises important questions about the interface between obsessive-compulsive disorder and body dysmorphic disorder (a preoccupation with an imagined defect in appearance). Published cases of compulsive face picking (1) have conceptualized this behavior as a form of obsessive-compulsive disorder. To our knowledge, Dr. Tanquary and colleagues are the first to note a relationship between compulsive face picking and body dysmorphic disorder.

We, too, have noted a relationship between compulsive face picking and body dysmorphic disorder. In our ongoing study of body dysmorphic disorder, we have encountered nine patients (four women and five men) with repetitive, time-consuming face picking. Eight of nine patients considered this behavior to result from their body dysmorphic disorder, which in seven cases consisted of typical preoccupations with imagined or minimal acne. The eighth case was less typical; like Dr. Tanquary's patient, the patient picked to remove imagined pus from beneath her skin to prevent it from surfacing on her skin and making her ugly. In some cases, the picking caused actual mild facial scarring, which intensified the body dysmorphic disorder symptoms. The ninth patient, unlike the others, considered her face picking to be primary; i.e., not a reaction to her body dysmorphic disorder. Instead, the mild resulting disfigurement caused body dysmorphic disorder symptoms.

Is repetitive face picking best conceptualized as body dysmorphic disorder or as obsessive-compulsive disorder? Is it sometimes the former and sometimes the latter? Unlike Dr. Tanquary and his colleagues, we consider the face picking of eight of our nine patients to be a symptom of their body dysmorphic disorder. This behavior was a response to a preoccupation with an imagined or greatly exaggerated "defect" in their appearance. Thus, repetitive face picking appears to be one of the many ritualistic behaviors that can occur in body dysmorphic disorder, which include repetitive mirror checking, persistent questioning or requests for reassurance, and repetitive grooming behaviors, such as hair combing or makeup application. Although certain repetitive—and sometimes self-mutilatory—grooming behaviors have been conceptualized as a form of obsessive-compulsive disorder (trichotillomania, compulsive hand washing, and onychophagia [nail biting] in humans [2]; compulsive paw licking in dogs [canine acral lick]; and feather picking disorder in birds [3]), some compulsive grooming behaviors (e.g., hair arranging and face picking) should, in some instances, be considered a complication of body dysmorphic disorder.

But what about the relationship between obsessive-compulsive disorder and body dysmorphic disorder themselves? Might they be related or even the same disorder? The answer to this question is unknown, but it appears that these disorders may be related, given their similar early age of onset, often chronic course, apparent high comorbidity with mood and anxiety disorders, substantial functional impairment and similar phenomenology—both consisting of persistent, intrusive

thoughts that are difficult to resist as well as compulsive, ritualistic behaviors (4). In addition, preliminary evidence suggests that body dysmorphic disorder may, like obsessive-compulsive disorder, respond to treatment with serotonergic antidepressants (5, 6). On the other hand, there appear to be differences between these two disorders. In our experience, patients with body dysmorphic disorder are less likely than those with obsessive-compulsive disorder to have insight into the senselessness of their preoccupations; that is, their preoccupations are more likely to consist of overvalued ideas or delusional thinking. It also appears that the ritualistic behaviors of body dysmorphic disorder, such as repetitive mirror checking, are less likely to temporarily relieve anxiety. Body dysmorphic disorder also appears to often cause more social impairment and isolation. Research is needed to confirm these impressions and to further explore the interface between these two disorders.

Most of our patients were extremely reluctant to discuss either their body dysmorphic preoccupations or their compulsive face picking and did so only when asked about them. Thus, it is important that clinicians specifically inquire about the presence of compulsive face picking in body dysmorphic patients and about body dysmorphic disorder in compulsive face pickers. Body dysmorphic disorder often has serious consequences, including social isolation, unemployment, hospitalization, and suicide—associated features that go beyond simple face picking and are important for clinicians to be aware of.

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KATHARINE A. PHILLIPS, M.D.
SUSAN L. MCELROY, M.D.
Belmont, Mass.

Simple Schizophrenia, Negative Symptoms, and Prefrontal Hypodopaminergia

SIR: Kenneth L. Davis, M.D., and associates (1) have reviewed evidence suggesting that schizophrenia is characterized by subcortical hyperdopaminergia and prefrontal hypodopaminergia. It is likely that this conception of the role of dopamine in schizophrenia will generate a great deal of research and stimulate new treatment approaches.

An especially provocative component of this hypothesis is that prefrontal hypodopaminergia is associated with the development of negative symptoms. There are two approaches to research on the treatment of schizophrenia that have provided

data consistent with this hypothesis and that have the potential to refine our understanding of hypodopaminergia in schizophrenia. One of these involves the use of dopamine precursors and agonists in the treatment of schizophrenia spectrum disorders such as schizoid or schizotypal personality, in which negative symptoms can be especially prominent (1). As yet, neither schizoid nor schizotypal personality disorder has been studied in this way. However, a beneficial effect of L-dopa has been reported in a double-blind crossover trial examining patients with simple schizophrenia (2). Simple schizophrenia is a subtype of schizophrenia defined by the absence of delusions and hallucinations and a corresponding predominance of negative symptoms. The results of this study are therefore consistent with the hypothesis that hypodopaminergia underlies negative symptoms. Although this study does not appear to have stimulated additional trials of dopaminergic agents in simple schizophrenia, diagnostic criteria for this subtype that could facilitate such research have been proposed (3, 4).

A second approach to investigating prefrontal hypodopaminergia examines dimensions of positive and negative symptoms rather than subtypes. In such research, patients are assessed on both of these symptom dimensions and their response to trials of dopamine precursors or agonists are evaluated. Based on the hypothesis that hypodopaminergia underlies negative symptoms, it can be predicted that negative symptoms will demonstrate a greater beneficial response to dopamine agonists than positive symptoms. Such an effect has been reported in trials of L-dopa (5) and amphetamine (6) in patients with schizophrenia.

Research on the effects of dopamine agonists in schizophrenia would be more informative if selective mesocortical dopamine receptor agonists were studied, for example, selective D₁ agonists (1). In such studies, it will also be important to examine separately negative symptoms and interpersonal deficits, a distinction with important theoretical and empirical implications that has often been neglected in research on negative symptoms.

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LEWIS A. OPLER, M.D., PH.D.
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Dr. Davis and Associates Reply

SIR: Dr. Dworkin and Dr. Opler call particular attention to the possibility that prefrontal hypodopaminergia is associated

with the development of negative symptoms, and that these can be treated with L-dopa. We heartily agree that patients within the schizophrenia spectrum who are relatively devoid of positive symptoms might benefit from trials that enhance dopaminergic activity. Obviously a major question that ultimately must be addressed is the most effective agent to use for selective augmentation of dopaminergic activity in cortical regions. Although L-dopa remains an interesting possibility, it surely will be increasing noradrenergic activity as well. This may, or may not, be beneficial. Dopamine agonists offer another approach, but the ideal dopamine receptor to activate, as well as how to maximize regional selectivity, remains a pharmacological dilemma.

One interesting approach to this problem has been the administration of the dopamine reuptake blocker mazindol. As recently reported (1), mazindol in combination with neuroleptics in a naturalistic outpatient setting was able to substantially reduce negative symptoms. This is an interesting approach that deserves further attention, particularly if, in combination with neuroleptics, mazindol may have a unique effect on cortical dopaminergic neurons.

A critical element in our reconceptualization of the role of dopamine in schizophrenia is the bidirectionality of dopamine. Hypodopaminergia in the cortex may be associated with hyperdopaminergia in subcortical regions. Recently this possibility received some support from a study in which cerebral blood flow was measured by single photon emission computed tomography. Schizophrenics following the Wisconsin Card Sorting Test were found to have diminished frontal cortical blood flow and increased striatal blood flow compared to control subjects completing the same task (2). The mechanism that may lead to such bidirectionality has received considerable attention at the preclinical level (unpublished paper by A.Y. Deutsch). An excitatory glutamatergic tract whose activity is diminished following cortical hypofunction may serve to mediate subcortical hypodopaminergia. Thus, isolation of the glutamatergic receptor subtype that modulates this subcortical dopaminergic response is clearly of interest and may offer an approach to the treatment of schizophrenia.

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Prevalence of Substance Abuse or Dependence Diagnoses on an Inpatient Inner City Psychiatric Unit

SIR: The 40% prevalence of substance abuse in psychiatric patients cited in a letter by Edward B. Gogek, M.D. (1), and in studies done by Crowley et al. (2) is relatively high; however, it is much lower than in the population I serve. Dr. Gogek's letter prompted me to review 50 consecutive discharges in the first half of 1991 from my acute inpatient general psychiatry service.

The center is a comprehensive state community mental health center with acute inpatient units in the inner city, serving a socially disadvantaged catchment area of over 160,000. The facility's policy is not to admit those with a primary diagnosis of substance abuse disorder or those with private health insurance or government medical assistance. I was not the admitting psychiatrist but I was the attending psychiatrist of all patients studied.

The prevalence of a substance abuse or dependence disorder on discharge (dually diagnosed) was 70%. Sixty-six percent of the patients were male; the median age was 33.2 years (only five patients were older than 45); 70% were Afro-American, 28% white, and 2% Native American. Almost all were currently unmarried. Seventy-six percent of the men had substance abuse diagnoses versus 59% of all women. Sixty-three percent of the Afro-Americans, 79% of the whites, and the one Native American had substance abuse diagnoses. The median age of the substance abusers was 32.7 years; median age of the nonsubstance abusers was 34.4 years. Excluding substance abuse diagnoses, principal diagnoses were schizophrenia, schizophreniform, or schizoaffective disorder in 30% (N=15) of the patients; organic mental disorder in nine patients; bipolar disorder in eight patients; psychosis, not otherwise specified in six patients; unipolar depression in three patients; substance dependence diagnosis in one patient; and other diagnoses in eight patients.

This study supports findings that "being younger, male, non-married, and of a lower socio-economic status" are associated with increased alcohol or other drug use (3). My population differs from that of Dr. Gogek's in that it is an inner city inpatient population. As patients with dual diagnoses are "less able to manage their lives in the community" than those with mental illness alone, one would expect a higher percentage of substance abuse diagnoses in those acutely hospitalized (4). Safer (5) found persistent substance abusers had a psychiatric hospitalization rate greater than 2.5 times higher than patients who had a past but not current history of substance abuse and patients with little or no substance abuse history. Also, I cite a figure over twice that of Crowley in his late 1971 sample of 50 consecutive admissions (2). Since that time there has been an increase in recognition and in absolute numbers of those with dual diagnoses (e.g., Crowley's study was before the crack cocaine epidemic).

Treatment studies generally exclude subjects with additional diagnoses, but this is not true in practice, where patients can present with a number of disorders. Regier (6) cites results from the ECA study that among those with a mental disorder, the odds ratio of having some addictive disorder was 2:7. In fact, 60.7% of patients with bipolar I disorder have a dual diagnosis; so it is the exception rather than the rule to find a person with bipolar I disorder without a substance abuse diagnosis (6).

Psychiatrists must be alert to substance abuse in their patients. Outside sources for historical material and perhaps toxicology screens "should be more systematically obtained," especially in hospitals where young adult chronic patients are evaluated (5). We must be cautious in diagnosing "functional" psychosis or other diagnoses when substance abuse is involved.

Importantly, the high prevalence rate of dual diagnoses brings sharply into focus the need for professionals, psychiatrists and others, to be well-trained in dealing with this population.

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DANIEL D. STORCH, M.D.
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Dr. Gogek Replies

SIR: Dr. Storch has brought up several important aspects of the interface between psychiatry and substance abuse treatment. First is a marked variability in the rates of substance abuse among psychiatric populations. Dr. Storch's rate of 70% is nearly twice the 40% reported in my letter. However he enumerated several demographic factors that contributed to this higher rate. His data support the contention that substance abuse occurs at higher rates in psychiatric populations than in the general population.

Second is that these high rates occur in psychiatric facilities with a policy not to treat patients with primary substance abuse diagnoses. While such a policy is often reasonable and necessary (e.g., for insurance purposes or to prevent psychiatric units from turning into detoxification units), it can lead to seemingly absurd situations, such as on Dr. Storch's unit, where, despite this policy, substance abuse is the most common diagnosis. It would be more accurate to state that the policy is not to admit patients whose only primary psychiatric diagnosis is substance abuse. Otherwise, it misleads clinicians by saying that they are not treating primary substance abuse disorders. Dr. Storch's data and my own show that this is not true. Both of our samples had high rates of primary substance abuse disorders.

Third, Dr. Storch says we need to be alert to substance abuse among our patients. I strongly concur. For this reason, surveys showing the prevalence of substance abuse among various psychiatric populations are very useful.

EDWARD B. GOGOK, M.D.
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Blunting Growth Hormone Release in Mania

SIR: We take issue with three statements made in the report by Timothy G. Dinan, M.D., and associates (1). First, they stated that growth hormone (GH) responses to clonidine and desmethylinipramine have not previously been studied in mania, but they have overlooked a number of findings. Ansseau et al. (2) found blunted responses to clonidine in groups of patients meeting Research Diagnostic Criteria for mania and major depression, compared with minor depression. Blunted GH responses to clonidine in mania were also found by Watanabe et al. (3).

Second, we disagree that blunted GH responses to noradrenergic stimulation are a "marker for affective disorder." The sensitivity of such testing is limited. The authors' own study with desmethylimipramine found blunting (<5 ng/ml increase) in only 48% of DSM-III-R-diagnosed patients with major depression (4). Specificity is questionable, given that blunted responses have been reported in generalized anxiety, panic and obsessive-compulsive disorders, Alzheimer's disease, alcoholism, and essential hypertension (5, 6).

Third, although the action of desmethylimipramine on GH is mediated by α_2 -adrenoceptors, it does not follow that blunting indicates their down-regulation. Several groups have shown decreased GH responses to growth hormone-releasing hormone (GH-RH) in depression and panic disorder, making interpretations of neurotransmitter sensitivities problematic.

Tests of noradrenergic receptor sensitivity that allow measures of presynaptic function (noradrenaline and 3-methoxy-4-hydroxyphenylglycol release, cardiovascular and sedation responses) may be more informative than the sole report of postsynaptic responses permitted by using the reuptake blocker desmethylimipramine. Simultaneous measurement of somatomedin C may throw some light on factors influencing pituitary responsiveness, but the difficulties of measuring somatostatin input and GH-RH remain a barrier to understanding the mechanisms in patients.

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Dr. Dinan and Associates Reply

SIR: Regarding the comments of Dr. Coupland and Dr. Glue, we accept that Ansseau et al. previously reported on clonidine/growth hormone responses in mania. We were unaware until recently of this publication.

In our inpatient population the sensitivity of the desipramine/growth hormone stimulation test is around 70% in the diagnosis of major depression. We have previously questioned the specificity of the test, reporting significant blunting in patients with irritable bowel syndrome (1) and alcoholism (unpublished). We do not accept that patients with obsessive-compulsive disorder show such blunting (2).

The release of growth hormone from the anterior pituitary is under complex control. Following the stimulation of noradrenergic receptors there is clearly a cascade of biochemical processes preceding the release of growth hormone. Blunted release in depression may be due to abnormalities at any point in the cascade. Down-regulation of noradrenergic α_2 -receptors is just one possible interpretation of the data.

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TIMOTHY G. DINAN, M.D.
SIOBHAN BARRY, M.B.
VERONICA O'KEANE, M.B.
LAKSHMI N. YATHAM, M.B.
Dublin, Ireland

Reprints of letters to the Editor are not available.

Correction

The address for Lawrence A. Labbate, M.D., author of the letter "Nicotine Cessation, Mania, and Depression" (May 1992 issue, p. 708), is Bremerhaven, Germany.

Highlights of the 145th Annual Meeting

The 145th Annual Meeting of the American Psychiatric Association was held in Washington, DC, May 2-7, 1992. The total registration was 14,704, including 7,764 members; 1,616 spouses, other family members, and guests; 3,589 nonmembers; 1,261 exhibitors; 220 members of the media; and 254 staff members.

Business Meeting

The Annual Business Meeting was called to order by Lawrence Hartmann, M.D., in the Washington Convention Center on Sunday, May 3, at 12:30 p.m.

First Session. Richard M. Bridburg, M.D., Recorder, announced the presence of a quorum. Dr. Hartmann then asked the audience to observe a moment of silence in memory of all members and Fellows who died during the past year. John Zinner, M.D., chairperson of the Committee of Tellers, announced the results of the election of officers and trustees. The reports to the membership followed. Steven S. Sharfstein, M.D., presented the Secretary's report, which was followed by the reports of Mary Jane R. England, M.D., Treasurer; Thomas Pfaffler, M.D., Speaker of the Assembly; Ronald A. Shellow, M.D., Speaker-Elect of the Assembly; Henry E. Payson, M.D., chairperson of the Committee on the Constitution and By-Laws; and Aron S. Wolf, M.D., chairperson of the Membership Committee. Melvin Sabshin, M.D., presented the Medical Director's report. Reports of all the councils were also available. All reports were accepted by the membership as submitted and will be published in the October 1992 issue of the *American Journal of Psychiatry*. Dr. Hartmann then recessed the first session of the business meeting.

Second Session. Following the business meeting Dr. Hartmann called the Annual Forum, for all voting members, to order. Dr. Hartmann opened the Forum and recognized Dr. Nathaniel Lehrman, from the Nassau County District Branch. Dr. Lehrman addressed the body with his intention to appeal his Medicaid fraud conviction. He also notified the body of his leadership in a psychiatric survivors group workshop. Dr. Hartmann then recognized Dr. Lester Shapiro, from Area II. Dr. Shapiro addressed the body and broached the subject of an approved action paper from the November 1991 Assembly meeting entitled, "Avoiding APA Conflict of Interest." He inquired whether there was a report on this paper. His request was referred to Ms. Jeanne Robb, Director, Office to Coordinate the Board and Assembly. Dr. Shapiro then spoke of another November 1991 paper on Industry Sponsored Symposia. This paper had been referred to the Scientific Program Committee. Dr. Sabshin addressed Dr. Shapiro's concern and noted that several Industry Sponsored Symposia had been turned down for the 1992 Annual Meeting due to topic and/or speaker overlap. Dr. Shapiro quoted a *Psychiatric News* article stating the financial connection between the APA Office of Education and Abbott Laboratories. Dr. Sabshin again addressed Dr. Shapiro's concerns and assured him that the monies obtained from Abbott Labs was through an educational grant and did not obligate APA or its Office of Education in any way to Abbott Labs. Lastly, Dr. Shapiro questioned the propriety of APA Past Presidents connected with the Industry Sponsored Symposia on anxiety sponsored by the Upjohn Company. Dr. Lawrence Hartmann addressed Dr. Shapiro's concerns and assured him that the connection was justified within the proper

context. Dr. Hartmann then recognized Dr. Jim Stringham from the Illinois Psychiatric Society, Area IV. Dr. Stringham proposed the creation of a task force to deal with anger, hostility, and resentment as they directly affect the work of psychiatrists today. Dr. Hartmann suggested that this action be presented to the President-Elect, Dr. Joseph English, in written form. Dr. English did make note, however, that there had been no formation of new components within the last year due to existing financial conditions. Dr. Hartmann stated that the Joint Reference Committee would address this issue again.

The Annual Business Meeting and Forum were adjourned by Dr. Hartmann at 1:30 p.m.

Opening Session

The opening session was called to order by Lawrence Hartmann, M.D., 120th President of the Association, on Sunday evening, May 3, in the Washington Convention Center. Dr. Hartmann read a letter of greetings to the membership from The Honorable Sharon Pratt Kelly, Mayor of the District of Columbia.

Dr. Hartmann introduced those seated on the stage with him: the members of the APA Board of Trustees, the officers of the APA Assembly, and Past Presidents of the Association. Dr. Hartmann then recognized members of the audience, including the members of the Assembly Executive Committee; Past Speakers of the Assembly; Past Vice-Presidents of the Association; newly elected APA national officers, trustees, and Assembly officers; presidents of the APA district branches; and the chairpersons of APA councils, commissions, and joint commissions. He then thanked the members of the Assembly for their hard work and dedication.

Allan Tasman, M.D., chairperson of the Scientific Program Committee, and Jeffrey S. Akman, M.D., chairperson of the Local Arrangements Committee, were introduced and thanked by Dr. Hartmann; each then presented a brief report.

Dr. Hartmann then thanked and recognized the following distinguished representatives of psychiatric and other related organizations from the United States and abroad:

Representatives of Organizations in the United States: Anne Alonso, Ph.D., President, American Group Psychotherapy Association; Sheila G. Baler, Ph.D., President, American College of Mental Health Administration; Kathryn E. Barnard, Ph.D., R.N., President, National Center for Clinical Infant Programs; Ruth Tiffany Barnhouse, M.D., President, Association of Women Psychiatrists; Allan Beigel, M.D., President, Group for the Advancement of Psychiatry; Harvey Bluestone, M.D., President, American Board of Forensic Psychiatry, Inc.; Jack W. Bonner III, M.D., President, National Association of Private Psychiatric Hospitals; Gordon H. Bower, Ph.D., President, American Psychological Society; Juan C. Cabrera, M.D., President, Philippine Psychiatrists in America; C. Robert Cloninger, M.D., President, American Psychopathological Association; Rabbi Jeffrey Cohen, D.Min., President, Association of Mental Health Clergy; Richard L. Cohen, M.D., President, American Academy of Child and Adolescent Psychiatry; Bertram Cohler, Ph.D., President, American Orthopsychiatric Association; Suzanne Dandoy, M.D., President, American College of Preventive Medicine; John B. Davies, M.D., President, American Society of Psychoanalytic Physicians; Prakash Desai, M.D., President, Na-

tional Association of VA Chiefs of Psychiatry; Michael R. Dillon, Ed.D., President, American Association on Mental Retardation; Marvin G. Drellich, M.D., President, American Academy of Psychoanalysis; Margaret Duff, President, American Psychiatric Association Auxiliary; David L. Dunner, M.D., President, Society of Biological Psychiatry; Paul Errera, M.D., Director, Mental Health & Behavioral Sciences Service Department of Veterans Affairs; Gerald H. Flamm, M.D., President, American Association of Psychiatric Administrators; Barry S. Fogel, M.D., Director, American Neuropsychiatric Association; Marshall Forstein, M.D., President, Association of Gay and Lesbian Psychiatrists; Frederick J. Frese, Ph.D., President, National Mental Health Consumers Association; Desmond S. Fung, M.D., President, Association of Chinese American Psychiatrists; Marc Galanter, M.D., President, American Academy of Psychiatrists in Alcoholism and Addictions; Alma Rose George, M.D., President, National Medical Association; Judith H. Gold, M.D., President, American College of Psychiatrists; Stanislaw Golec, M.D., President, Association of Polish Psychiatrists and Neurologists in America; Lillian Gonzalez-Pardo, M.D., President, American Medical Women's Association, Inc.; Frederick K. Goodwin, M.D., Director, National Institute of Mental Health; Enoch Gordis, M.D., Director, National Institute on Alcohol Abuse and Alcoholism; Frederick G. Guggenheim, M.D., President, Association for Academic Psychiatry; Irwin N. Hassenfeld, M.D., President, Association of Directors of Medical Student Education in Psychiatry; Adolph Herath, M.D., President, Sri Lankan Psychiatrists in America; Helen S. Hintz, President, National Depressive and Manic-Depressive Association; G. Richard Holt, M.D., M.S.E., President, American Academy of Otolaryngology - Head & Neck Surgery; Lucille Joel, Ed.D., R.N., President, American Nurses' Association; Dale Johnson, President, National Alliance for the Mentally Ill; Richard F. Jones III, M.D., President, American College of Obstetricians and Gynecologists; Irwin Kopin, M.D., President, American College of Neuropsychopharmacology; Robert L. Leon, M.D., President, American Association for Social Psychiatry; Alan I. Leshner, Ph.D., Deputy Director, National Institute of Mental Health; Constance E. Lieber, President, National Alliance for Research on Schizophrenia and Depression; Richard C. Lippincott, M.D., President, National Association of State Mental Health Program Directors; Don R. Lipsitt, M.D., President, American Association of General Hospital Psychiatrists; Willis C. Maddrey, M.D., FACP, President, American College of Physicians; G. Alan Marlatt, Ph.D., President, Association for the Advancement of Behavior Therapy; Peter A. Martin, M.D., President, Benjamin Rush Society; Robert J. McAllister, M.D., Ph.D., President, National Guild of Catholic Psychiatrists; Charles McCafferty, M.D., President, American Society for Adolescent Psychiatry; Morris B. Mellon, M.D., President, American Academy of Family Physicians; Ricardo P. Mendoza, M.D., President, American Association for Emergency Psychiatry; Richard A. Millstein, Acting Director, National Institute on Drug Abuse; Christine Mitchell, R.N., M.T.S., President, American Society of Law & Medicine; Marianne H. Mitchell, Ed.D., President, American Association for Counseling and Development; David L. Nimmo, J.D., President, National Council of Community Mental Health Centers; Bernard L. Pacella, M.D., President, American Psychoanalytic Association; Ashwin Pandya, M.D., President, American Association of Psychiatrists from India; Walter A. Pedemonte, M.D., President, American Society of Hispanic Psychiatrists; Ghulam Qadir, M.D., President, Pakistan Psychiatric Society of America; Kathleen M. Quinn, M.D., President, American Academy of Psychiatry and the Law; Anthony B. Radcliffe, M.D., President, American Society of Addiction Medicine; Roger N. Rosenberg, M.D., President, American Academy of Neurology; Elisabeth Rukeyser, Chairman of the Board, National Mental Health Association; Abdel Aziz Salama, M.D., President, Arab American Psychiatrists Association of America; Raymond Scalettar, M.D., Secretary-Treasurer, American Medical Association; M. Ali Shamie, M.D., President, Society of Iranian Psychiatrists in North America; Daniel W. Shea, M.D., President, American Academy of Pediatrics; G. Pirooz Sholevar, M.D., President, Society of Professors of Child and Adolescent Psychiatry; Alan P. Siegal, M.D., President, American Association for Geriatric Psychiatry; Peter M. Silberfarb, M.D., President, American Association of Chairmen of Departments of Psychiatry; Michael A. Silver, M.D., President, American Association of Community Psychiatrists; Isaac Slaughter, M.D., President, Black Psychiatrists of America; James B. Smith, M.D., Presi-

dent, American Academy of Clinical Psychiatrists; W. Anderson Spickard, M.D., President, Association for Medical Education and Research in Substance Abuse; Christian L. Stephens, President, Association of Mental Health Administrators; Ralph A. Straffon, M.D., F.A.C.S., President, American College of Surgeons; Robert H. Taylor, M.D., President, Council of Medical Specialty Societies; Troy L. Thompson II, M.D., President, Academy of Psychosomatic Medicine; Gary J. Tucker, M.D., President, American Board of Psychiatry and Neurology, Inc.; Ulku Ulgur, M.D., President, Turkish-American Neuropsychiatric Association; Sidney H. Weissman, M.D., President, American Association of Directors of Psychiatric Residency Training, Inc.; Barbara W. White, Ph.D., President, National Association of Social Workers, Inc.; Roy Whitman, M.D., President, American College of Psychoanalysts; Jack G. Wiggins, Ph.D., President, American Psychological Association; and Redford B. Williams, Jr., M.D., President, American Psychosomatic Society, Inc.

International Scholars: Janine Chasseguet-Smirgel, Ph.D., training analyst in Paris; Inge Kemp Genefke, M.D., founder and Medical Director of the International Rehabilitation and Research Centre for Torture Victims in Copenhagen; George E. Mahy, M.B., an Associate Consultant Psychiatrist for the Barbados Ministry of Health at two public hospitals; Svetlana Polubinskaya, Ph.D., Senior Research Scholar, Department of Criminal Law and Criminology of the Institute of State and Law of the Russian Academy of Sciences in Moscow; Helmut Remschmidt, M.D., Director of the Department of Child and Adolescent Psychiatry at the Philipps-University in Marburg, Germany.

Representatives of Other International Organizations and Psychiatric Associations in Other Countries: Dr. Irving Philips, International Association of Child and Adolescent Psychiatry and Allied Professions; Dr. Sanford Finkel, International Psychogeriatric Association; Dr. Neal Cutler, International Association of Gerontology; Dr. Irene Jacob, International Society on the Psychopathology of Expression; Dr. Rodolfo Fahrner, InterAmerican Council of Psychiatric Organizations; Dr. Robert Pasnau, Pacific Rim College of Psychiatrists; Dr. A. Guilherme Ferreira, World Association of Social Psychiatry; Prof. Jorge Alberto Costa e Silva, World Psychiatric Association; Dr. Tim McKergow, Royal Australian and New Zealand College of Psychiatrists; Prof. Roger Montenegro, Argentine Psychiatrists' Association; Dr. Jacques Drouin, Canadian Psychiatric Association; Dr. Jiri Raboch, Czechoslovak Psychiatric Association; Dr. Fiona Caldicott, Royal College of Psychiatrists of Great Britain; Dr. C.R. Featherston, Canadian Psychoanalytic Society; Dr. Otto Doerr, Chilean Society of Neurology and Psychiatry; Dr. Roberto Chaskel, Colombian Society of Psychiatrists; Dr. Annette Gjerris, Danish Psychiatric Society; Dr. Carlos Leon Andrade, Ecuadorian Psychiatric Society; Prof. Ahmed Okasha, Egyptian Psychiatric Association; Dr. Antti Hemmi, Finnish Psychiatric Association; Prof. P. Cosyns, Flemish Association of Psychiatry and Neurology; Dr. Simon-Daniel Kipman, French Federation of Psychiatry; Prof. Uwe Henrik Peters, German Society of Psychiatry and Nervous Diseases; Dr. Felice Lieh-Mak, Hong Kong Psychiatric Association; Dr. Janos Furedi, Hungarian Psychiatric Association; Dr. Dadang Hawari, Indonesian Psychiatric Association; Dr. Charles Smith, Irish Division of the Royal College of Psychiatrists; Dr. Masahisa Nishizono, Japanese Psychoanalytic Association; Dr. Hajime Kazamatsuri, Japanese Society of Psychiatry and Neurology; Dr. Shigeru Kawasaki, Japanese Association of Psychiatric Hospitals; Dr. Dong-Il Kwak, Korean Neuropsychiatric Association; Dr. Chung Kyoon Lee, Korean Society of Biological Psychiatry; Dr. Charles Pull, Luxembourgian Association of Psychiatry; Prof. Frans G. Zitman, Netherlands Association for Psychiatry; Prof. Per Vaglum, Nordic Psychiatric Associations; Dr. Alv Dahl, Norwegian Psychiatric Association; Dr. Mohamed Chaudhry, Pakistan Psychiatric Society; Dr. Yuri Savenko, Independent Psychiatric Association of Russia; Dr. Lai H. Peh, Singapore Psychiatric Association; Dr. Ian Simon Fraser, Ministry of Health of South Africa; Dr. Somporn Bissaratid, Psychiatric Association of Thailand; Dr. Ruben Hernandez Serrano, Medical Federation of Venezuela; Dr. Antonio Pacheco Hernandez, Venezuelan Psychiatric Association.

APA Medical Director, Melvin Sabshin, M.D., introduced Dr. Hartmann, who gave the Presidential Address, "Reflections on Humane Values and Biopsychosocial Integration" (printed elsewhere in this issue of the *Journal*). Boris M. Astrachan, M.D., introduced Joseph English, M.D., President-Elect of the Association, who gave

the Response to the Presidential Address, "Patient Care for the Twenty-First Century" (printed elsewhere in this issue). Dr. Hartmann then adjourned the opening session.

Convocation

The 36th Convocation of Fellows was held in the Washington Convention Center beginning at 8:00 p.m. on Monday, May 4. Dr. Hartmann presided. After the processional march, Dr. Hartmann called the Convocation to order. President-Elect, Joseph English, M.D., then led the ceremony conferring Life Fellowship and the induction of Fellows of the Association.

Dr. Hartmann recognized the 1991 Corresponding Fellows: Leonardo A. Ancona, M.D., Rome, Italy; Ellis A.D. Busnello, M.D., Porto Alegre, Brazil; Char-Nie Chen, M.D., Shatin, Hong Kong; Hideo Hosaki, M.D., Tokyo, Japan; Simon-Daniel Kipman, M.D., Paris, France; Jochen E.F. Neumann, M.D., Ueckermunde, Germany.

The following 50-Year Life Fellows and Life Members (1942-1992) were then recognized: Freeman H. Adams, M.D., Stockton, CA; Justin H. Adler, M.D., Memphis, TN; C. Knight Aldrich, M.D., Charlottesville, VA; Herman S. Alpert, M.D., New York, NY; Louis Altman, M.D., Miami, FL; Herbert Jack Apfelberg, M.D., Palo Alto, CA; William C. Barger, M.D., Ft Lauderdale, FL; Frank R. Barta, M.D., Ocean Springs, MS; David Beres, M.D., Scarsdale, NY; Viola W. Bernard, M.D., New York, NY; Robert S. Berns, M.D., Los Angeles, CA; Irving Bieber, M.D., New York, NY; Walter R. Bonime, M.D., New York, NY; Morris V. Borenstein, M.D., New York, NY; Louis D. Boshes, M.D., Chicago, IL; Paul H. Brauer, M.D., New York, NY; S. George Brown, M.D., Milwaukee, WI; Howard B. Carscallen, M.D., London, ON, Canada; Stella Chess, M.D., New York, NY; Robert A. Clark, M.D., Elkins Park, PA; Joseph J. Doltolo, M.D., Brooklyn, NY; Maurice Dunn, M.D., Augusta, GA; Isaac C. East, M.D., Brandon, MS; Harmon S. Ephron, M.D., Fayetteville, NY; Knox H. Finley, M.D., Stinson Beach, CA; Joe E. Freed, M.D., Prosperity, SC; Moses M. Frohlich, M.D., Laguna Hills, CA; Samuel Futterman, M.D., Sebastopol, CA; Nicolai Gioscia, M.D., New York, NY; Leonard Gold, M.D., Stamford, CT; Charles Greenberg, M.D., Nyack, NY; John Howard Greist, M.D., Indianapolis, IN; William S. Hall, M.D., Columbia, SC; Lynwood Heaver, M.D., Tulsa, OK; Thomas V. Hoagland, M.D., Moore Haven, FL; John O. Hurt, M.D., Vinton, VA; William T. Hyslop, M.D., Traverse City, MI; Edward R. Janjigian, M.D., Kingston, PA; Edwin Kasin, M.D., New Rochelle, NY; S. Harvard Kaufman, M.D., Seattle, WA; Francis W. Kelly, M.D., Fairport, NY; James P. King, M.D., Radford, VA; Oscar Kozberg, M.D., Little Rock, AR; Harold J. Lawn, M.D., St. Paul, MN; Henry D. Lederer, M.D., West Chester, PA; Alexander H. Leighton, M.D., Halifax, NS, Canada; Robert J. Lentz, M.D., Laguna Hills, CA; Hans W. Loewald, M.D., New Haven, CT; Sydney B. Maughns, M.D., St Louis, MO; Michael Mendelson, M.D., Westbury, NY; Charles Samuel Mullin, M.D., Boston, MA; Thomas A. Naclerio, M.D., West Hempstead, NY; Richard W. Nelson, M.D., Worcester, MA; Leo Rangell, M.D., Los Angeles, CA; William Rottersman, M.D., Atlanta, GA; Jurgen Ruesch, M.D., San Francisco, CA; Bertram Schaffner, M.D., New York, NY; Manuel J. Scham, M.D., Yonkers, NY; Daniel E. Schneider, M.D., New York, NY; Julius Schreiber, M.D., Washington, DC; John P. Shovlin, M.D., Carbondale, PA; Werner Simon, M.D., Minneapolis, MN; S. Mouchly Small, M.D., Buffalo, NY; Stewart R. Smith, M.D., Brookline, MA; W. David Steed, M.D., Hinsdale, IL; Thomas W. Sugars, M.D., Bend, OR; John B. Train, M.D., Tamarac, FL; Ellsworth H. Trowbridge, Jr., M.D., Sun City, AZ; Walter I. Tucker, M.D., Wellestley, MA; Robert Joseph Van Amberg, M.D., Montclair, NJ; Bella S. Van Bark, M.D., New York, NY; Hewitt I. Varney, M.D., Annapolis, MD; Jack A. Vatz, M.D., Palm Springs, CA; George Leland Wadsworth, M.D., Waterloo, IA; Edward J. Weiss, M.D., New York, NY; Frederick L. Weniger, M.D., Pittsburgh, PA; Benjamin Wiesel, M.D., Hartford, CT; Isadore S. Zfass, M.D., Richmond, VA.

Dr. Hartmann then presented Honorary Fellows, Dr. Jean Endicott (in absentia), Mrs. Patricia Kind, and Dr. Rachel Gittelman Klein, and Distinguished Fellow, Dr. Leo E. Hollister, with their fellowship medallions.

Dr. Hartmann introduced The Honorable Edward M. Kennedy (D-MA), United States Senate. Senator Kennedy gave the William C. Menninger Memorial Convocation Lecture.

Special Presidential Commendations were presented to Leon Eisenberg, M.D., "in appreciation of his many decades of high intelligence, hard work, scientific skepticism, and social consciousness on behalf of children, public health and social policy"; to Erik H. Erikson (in absentia), "in appreciation for a generative lifetime of loving, working and playing; of science, art and wisdom"; to Jeanne Spurlock, M.D., "a tough and gentle inspiring colleague, and a good mother to children of all ages"; and to The Mental Health Law Project, "in recognition of its 20 years of advocacy and on the occasion its new name honoring Judge David L. Bazelon, a pioneer in the field of psychiatry and the law." This award was accepted by Mr. Leonard Rubenstein, Executive Director of the Project, and Mr. Richard Bazelon, son of Judge David L. Bazelon.

Distinguished Service Awards were presented to Albert J. Solnit, M.D., Commissioner of Mental Health for the State of Connecticut; and to Eli Robins, M.D., a faculty member of the Washington School of Medicine; and the Institutional Distinguished Service Award was presented to the American College of Neuropsychopharmacology, and was accepted by Roger Meyer, ACNP President-Elect. This award was established by the Board of Trustees in 1964 to honor APA members who have contributed exceptional meritorious service to American psychiatry, and to groups which have benefitted the APA, the field of psychiatry, or the mentally ill.

After introducing the chairpersons of the award committees, Dr. Hartmann presented the 1992 awards.

W. Walter Menninger, M.D., President, Chief Executive Officer and Chief of Staff of the Menninger Clinic in Topeka, Kansas, received the Administrative Psychiatry Award. Established in 1983, this award honors an APA member who is a nationally recognized clinician executive, whose effectiveness as an administrator of major mental health programs has expanded the body of knowledge of management in the mental health services delivery system, and whose effectiveness has made it possible for them to function as a role model for other psychiatrists.

The APA Award for Research in Psychiatry, formerly the Foundations' Fund Prize for Research in Psychiatry, the highest award for research given by the APA, was awarded to Judith H.L. Rapoport, M.D., Chief of the Child Psychiatry Branch of the NIMH.

The APA Award for Research Development in Hospital Psychiatry, given to honor outstanding contributions in hospital psychiatry research, was presented to Leona Bachrach, Ph.D., Research Professor of Psychiatry at the Maryland Psychiatric Research Center, University of Maryland School of Medicine.

The APA/Dista Products Resident Research Award, established in 1985 to honor a psychiatry resident for excellence in research undertaken during residency, was presented to Gianni L. Faedda, M.D., a psychiatry resident at McLean Hospital in Belmont, MA; to Glenn N. Saxe, M.D., a psychiatry resident at Harvard University Medical School at Massachusetts Mental Health Center/Massachusetts General Hospital; to Stephen M. Strakowski, M.D., the chief resident in the Psychiatric Disorders Program, Howard University Medical School; to J. Randolph Swartz, M.D., a psychiatry intern and resident at Harbor-UCLA Medical School; and to Debby W. Tsuang, M.D., a resident-in-training at the University of Iowa Hospitals and Clinics.

The APA/Wisniewski Young Psychiatrist Research Award, established in 1990 in honor of the late Dr. Alexander A. Wisniewski to recognize significant research accomplishments or promise of young psychiatrists, was presented to James T. McCracken, M.D., Assistant Professor of Psychiatry at the UCLA School of Medicine.

The Francis J. Braceland Award was presented to Harvey L. Ruben, M.D., Chairperson of the APA's Joint Commission on Public Affairs and host of the radio call-in show, "Talknet." This award was established in 1977 to honor a member of the Association who has made outstanding contributions as an author, spokesperson and publicist in the service of the mentally ill and disabled, and to the art and science of helping them.

The Marie H. Eldredge Award, established in 1964 to honor an APA member or resident residing and working in Hawaii, Pennsylvania, or New Jersey, and recognizing research work into the cause and treatment of neuroses and retardation, was presented to Duncan B. Clark, M.D., Assistant Professor of Psychiatry at the Western Psychiatric Institute and Clinic, University of Pittsburgh.

The Samuel G. Hibbs Award was presented to Evelyn Albrecht

Schwaber, M.D., Training and Supervisory Analyst at the Psychoanalytic Institute of New England, East, for her paper entitled "Psychoanalytic Theory and Its Relation to Clinical Work." This award is given for the best unpublished paper on a clinical subject.

The Human Rights Award was presented for the first time this year to the Science and Human Rights Program and the Committee on Scientific Freedom and Responsibility of the American Association for the Advancement of Science. The award was accepted by Robert Kirschner, M.D., Chairperson of the AAAS Committee on Scientific Freedom and Responsibility. This award was established in 1990 to recognize an individual or organization exemplifying the capacity of human beings to protect others from damage related to the professional, scientific, and clinical dimensions of mental health, at the hands of other human beings.

The Blanche F. Ittleson Award for Research in Child Psychiatry, given to a child psychiatrist or group of investigators for published results of research pertaining to the mental health of children, was presented to David B. Herzog, M.D., Associate Professor of Psychiatry, Harvard Medical School.

The Kempf Fund Awards for Research Development in Psychobiological Psychiatry were presented to Daniel C. Javitt, M.D., who was a resident in the Albert Einstein College of Medicine/Montefiore Medical Center combined program, and is now Assistant Professor, Department of Psychiatry and Neuroscience, Albert Einstein College of Medicine, to honor a resident who demonstrates exceptional promise in psychiatric research; and to Stephen R. Zukin, M.D., Professor, Department of Psychiatry and Neuroscience, Albert Einstein College of Medicine of Yeshiva University, to honor research excellence in the psychobiological, psychological, and/or sociological causes and treatment for the mental disease known as schizophrenia.

Saul I. Harrison, M.D., Professor Emeritus at the University of Michigan, received the Agnes Purcell McGavin Award, given to honor a psychiatrist who has done and is currently doing outstanding work related to the preventive aspects of the emotional disorders of childhood, through framing concepts, developing proofs or creating applications.

The Robert T. Morse Writers Award, which honors popular writers who have made major contributions to the public understanding of psychiatry and mental illness, was presented to Felice J. Freyer (in absentia), medical writer for the *Providence Journal-Bulletin*.

Dr. Paulos Mar Gregorios, an internationally known religious thinker and writer, and former President of the World Council of Churches, received the Oskar Pfister Award, given to honor outstanding contributions in the field of psychiatry and religion.

The Isaac Ray Award, given to those who have made outstanding contributions to forensic psychiatry or to the psychiatric aspects of jurisprudence, was presented to The Honorable Harry A. Blackmun, United States Supreme Court Justice since 1970.

The Robert L. Robinson Award was given to KOCO-TV staff in Oklahoma City: Jack Ahearn (in absentia), chief news photographer; Jane Braden, health reporter; Ann Parrington (in absentia), news photographer; and Gary A. Wolfe (in absentia), news photographer, for their outstanding work on the KOCO-TV "State of Mind" program; and to Catherine Olian (in absentia), producer, and Lesley Stahl (in absentia), Co-Editor, for "60 Minutes" for their outstanding work on the CBS News 60 Minutes "Prozac" program. The Robert L. Robinson Award recognizes radio and television (including cable) productions that contribute significantly to a better public understanding of psychiatry and mental illness.

The Arnold L. van Ameringen Award in Psychiatric Rehabilitation was presented to Arthur T. Meyerson, M.D., Professor of Psychiatry and Chairman of the Department of Psychiatry and Mental Health Sciences at the Hahnemann University School of Medicine in Philadelphia, for his outstanding contributions to the field of psychiatric rehabilitation, in the areas of clinical service, research, education, advocacy or a combination thereof.

The Seymour D. Vestermark Award, which recognizes an educator who has made outstanding contributions to undergraduate, graduate, or postgraduate education and career development in psychiatry, was presented to Carol C. Nadelson, M.D., Director of Training and Education for the Department of Psychiatry at the New England Medical Center in Boston and Professor of Psychiatry and Vice Chair of Academic Affairs at Tufts University School of Medicine.

The Jack Weinberg Memorial Award for Geriatric Psychiatry was

presented to Dan G. Blazer, M.D., Director of the Affective Disorders Program at Duke University Medical Center. This award honors a psychiatrist who has demonstrated special leadership or who has done outstanding work in clinical practice, training or research into geriatric psychiatry anywhere in the world.

After the presentation of these awards, Dr. Hartmann adjourned the Convocation.

Awards presented at meetings or sessions other than the Convocation included the following:

District Branch Newsletter of the Year Awards, given to recognize excellence in achievement and honor those newsletters and their editors that have most effectively communicated with the District Branch membership. The award for Large District Branches was presented to the *Massachusetts Psychiatric Society News*, Eileen B. Kahan, M.D., Editor; and to the *Wisconsin Psychiatrist*, Gilbert B. Tybring, M.D., and Richard J. Thurrell, M.D., Editors; and for Small District Branches, *SYNAPSE*, Robert N. Sobel, M.D., and Syed Abdullah, M.D., Editors. The Continuing Excellence Award was presented to *APS Action*, James F. Hooper, M.D., Editor; *Connecticut Psychiatrist*, Boris G. Rifkin, M.D., Editor; *Pennsylvania Psychiatrist*, Lee Miller, M.D., Editor; and the *Washington Psychiatric Society Newsletter*, Harold I. Eist, M.D., Editor.

The first annual Asian/Asian American Award was presented to Tsung-yi Lin, M.D., Honorary President of the World Federation of Mental Health, and to Lindbergh S. Sata, M.D., Chairman of the Department of Psychiatry and Human Behavior at St. Louis University. This award is given to recognize significant contributions toward understanding the impact and import of Asian cultural heritages in areas relevant to psychiatry, to encourage scholarship and research in culture-specific mental health issues and treatment needs of Asian populations and to stimulate scientific exchange on transcultural issues.

The Manfred S. Guttmacher Award, given to honor outstanding contributions to the literature of forensic psychiatry, was given to James C. Beck, M.D., Director of the Cambridge Court Clinic and Chief of Forensic Psychiatry at Cambridge Hospital.

The Lilly Psychiatric Research Fellowship was awarded to Shitij Kapur, M.D., a fourth-year resident in the Laboratory of Neuropharmacology at the Western Psychiatric Institute and Clinic, University of Pittsburgh. The fellowship was established to provide support for the career development of a postgraduate medical trainee who has shown exceptional promise in psychiatric research.

The Adolf Meyer Award honors outstanding investigators and was awarded to George L. Engel, M.D., Professor Emeritus of Psychiatry and Medicine at the University of Rochester in New York.

The Award for Patient Advocacy, which recognizes a public figure respected for personal accomplishments and beliefs, who has promoted the improvement of services for people coping with mental disorders and substance abuse, and who has fought stigma by speaking out about experiences with mental illness and psychiatric treatment, was awarded to Pulitzer Prize-winning author, William Styron.

The Benjamin Rush Award, which honors an individual who has achieved renown for his/her contribution to the history of psychiatry from that field or other fields such as medical history, anthropology or sociology, was awarded to Aaron Lazare, M.D., Chancellor of the University of Massachusetts Medical Center, Worcester.

The Simon Bolivar Award, which is given to honor a prominent Hispanic statesman or spokesperson, was awarded to Raquel E. Cohen, M.D., Professor of Psychiatry and Adjunct Professor of Pediatrics at the University of Miami School of Medicine.

Gloria Johnson-Powell, M.D., Professor of Child Psychiatry at the Harvard Medical School, received the Solomon Carter Fuller Award, given to honor a Black citizen who has pioneered in an area which has significantly benefitted the quality of life for Black people.

The Jacob K. Javits Public Service Award, which honors a public servant who has made a significant contribution to the cause of the mentally ill, was received by Minnesota State Representative Gloria M. Segal.

Scientific Sessions

The Scientific Program began on Monday, May 4, but continuing medical education (CME) courses and industry sponsored symposia began on Saturday and Sunday, May 2-3. There were 22 discussion

groups; nine forums; 122 symposia; 27 industry sponsored symposia; two special presidential symposia; 628 new research presentations; two debates; one "round table discussion"; 121 papers presented in 40 paper sessions; 172 workshops (including 58 APA component presentations and 114 issue); 15 film sessions; 32 videotape sessions and three video production clinics; 122 CME courses; four medical updates; five review of psychiatry sessions; four clinical case conferences; two, two-part continuous clinical case conferences; three "research consultation with . . ." sessions; and 11 "clinical consultation with . . ." sessions. Other sessions included "Research Advances in Psychiatry: An Update for the Clinician"; "Workshops on Private Practice Issues"; the residents' session, "Meet the Experts: Sunny-Side Up"; the ADAMHA Workshop; the DSM-IV Update; the Public Symposium; the Social Security Workshop; and an AIDS Education Program.

There were 31 lectures presented. The speakers, their current positions, and the titles of their presentations are listed here.

On Sunday, May 3, a lecture was given by James C. Beck, M.D., Director of the Cambridge Court Clinic, Chief of Forensic Psychiatry at Cambridge Hospital and Associate Professor of Psychiatry at Harvard Medical School, "The Death Penalty, Race and Psychiatry."

On Monday, May 4, the following speakers gave lectures: Evelyn Albrecht Schwaber, M.D., Training and Supervisory Analyst at the Psychoanalytic Institute of New England, East, "Psychoanalytic Theory and Its Relationship to Clinical Work"; Dr. Svetlana Polubinskaya, Senior Research Scholar in the Department of Criminal Law and Criminology of the Institute of State and Law of the Russian Academy of Sciences in Moscow, "From the USSR to the Independent States: Where the Former Soviet Psychiatry Will Go"; M. Scott Peck, M.D., author of the best-selling book, *The Road Less Traveled* and nationally recognized authority on the relationship between religion and science, "Biopsychosocialspiritual Psychiatry: What is Psychiatry to Do About Spirituality?"; Raquel E. Cohen, M.D., Professor of Psychiatry and Adjunct Professor of Pediatrics at the University of Miami School of Medicine and Director of the Children's Center of the Office of the State's Attorney in the 11th Judicial Circuit of Florida, "Twenty Years and Twenty Post-Trauma Clinical Lessons: From Macro Events to Micro Application"; Stanley J. Watson, M.D., Associate Director of the Mental Health Research Institute and Professor and Research Scientist in the Department of Psychiatry at the University of Michigan in Ann Arbor, "The Dopamine Receptor Super-Family and Its Implications for Psychiatry"; William Styron, 1968 Pulitzer Prize-winning author of *The Confessions of Nat Turner*, "Depression and the Creative Process"; Eric Lander, D. Phil., Associate Professor of Biology at the Massachusetts Institute of Technology and Director of the MIT Center for Genome Research, "Human Genetics and the Human Genome Project: Scientific and Social Implications"; Helmut Remschmidt, M.D., Managing Director of the Center of Neurology and Psychiatry and Director of the Department of Child and Adolescent Psychiatry at the Philipps-University in Marburg, Germany, "Research Fields and Strategies in Developmental Psychopathology"; Otto F. Kernberg, M.D., Associate Chairman and Medical Director of the New York Hospital-Cornell Medical Center, Westchester Division, and Professor of Psychiatry at Cornell University Medical College in New York, "Masochism: Psychopathology and Clinical Observations"; Senator Edward M. Kennedy, (D-MA), Convocation Lecture.

On Tuesday, May 5, the following lectures were given: Dr. Paulos Mar Gregorios, internationally known religious thinker and writer, and former President of the World Council of Churches, "Religious Masters as Psychiatrists: The Threefold Role of Religion in the Healing of Mind, Body and Soul in Society"; James A. McDermott, M.D., US Representative (D-WA), "Perspectives of a Psychiatrist in Congress"; Inge Kemp Genefke, M.D., founder and Medical Director of the International Rehabilitation and Research Centre for Torture Victims in Copenhagen, "Torture: A Threat to Democracy, a Challenge to Psychiatry"; Charles Krauthammer, M.D., Pulitzer Prize-winning syndicated columnist, "America and the New World Order: Trials of a Lonely Superpower"; Hugh L. Freeman, D.M., Honorary Professor in the Department of Sociology and Anthropology at the University of Salford, England, "Mental Health and the Environment"; Frederick K. Goodwin, M.D., Director, National Institute of Mental Health,

"Conduct Disorder as a Precursor to Adult Violence and Substance Abuse: Can the Progression Be Halted."

On Wednesday, May 6, the following lectures were presented: Carol C. Nadelson, M.D., Past President of the American Psychiatric Association, Director of Training and Education for the Department of Psychiatry at the New England Medical Center in Boston and Professor of Psychiatry at Tufts University School of Medicine, "Ethics, Empathy and Gender in Health Care"; Paula J. Clayton, M.D., Professor and Head of the Department of Psychiatry, University of Minnesota Medical School, "Reactive Depression: Its Place in the Classification of Affective Disorder"; W. Walter Menninger, M.D., President, Chief Executive Officer and Chief of Staff of the Menninger Clinic in Topeka, Kansas, "Critical Elements in Organizational Function"; Professor Leo Steinberg, Professor Emeritus of the History of Art, University of Pennsylvania, "The Devil His Due: Who's Who in Michelangelo's Creation of Adam"; Gloria Johnson-Powell, M.D., Professor of Child Psychiatry at Harvard Medical School and Director of the Camille Cosby Ambulatory Care Center of the Judge Baker Children's Center in Boston, "Black Monday's Children: A Multi-Cultural Agenda for the 21st Century"; Dr. Janine Chasseguet-Smirgel, a training analyst in Paris and author, "Eating Disorders and Femininity"; Louis Joylon West, M.D., Professor of Psychiatry, UCLA School of Medicine and Director of the Preventive Psychiatry Center at UCLA, "Psychiatry and Scientology"; Stanley I. Greenspan, M.D., Clinical Professor of Psychiatry and Behavioral Sciences and of Pediatrics at George Washington University Medical School in Washington, D.C., and Supervising Child Psychoanalyst at the Washington Psychoanalytic Institute, "The Formation of the Mind: Implications for the Prevention of Autism and Disorders of Thought and Affect"; Martin Duberman, Ph.D., Distinguished Professor of History at the Graduate School and University Center of the City University of New York, "Cured: A Gay Man's Odyssey in Psychotherapy"; Stephen Jay Gould, Ph.D., Professor of Geology and of Zoology at Harvard University and Curator of Invertebrate Paleontology at Harvard's Museum of Comparative Zoology, "A Wonderful Life: The Pattern of Life's History and the Improbability of Human Evolution"; George E. Mahy, M.B., Senior Lecturer in Psychiatry, Faculty of Medical Sciences, University of the West Indies, Cave Hill Campus, Barbados, "Suicide and Attempted Suicide in a Developing Country: The Case of Barbados."

The lectures presented on Thursday, May 7, were: Aaron Lazare, M.D., Chancellor of the University of Massachusetts Medical Center in Worcester, "Shame and Humiliation in the Clinical Encounter"; David Dressler, Ph.D., Lecturer in Neurobiology, Harvard Medical School, "Thinking About Thinking: Recent Molecular Biological Insights into Learning and Memory"; Paula Tallal, Ph.D., Professor of Neuroscience and Co-Director of the Center for Molecular and Behavioral Neuroscience at Rutgers University in Newark, New Jersey and Adjunct Professor of Neurosciences at the University of Medicine and Dentistry of New Jersey-New Jersey Medical School, "Neurobiological Foundations of Language Development and Disorders."

Other Activities

The Committee on Local Arrangements, Jeffrey S. Akman, M.D., chairperson, planned many activities, among which were golf and tennis tournaments, biking, and birdwatching. Some of the tours included: Monuments by Moonlight, Behind Closed Doors - Historic Georgetown, Embassy Row and Georgetown, Monticello, Enchantment by the Bay, and Behind the Scenes: The United States Capitol.

Meeting of the Board of Trustees

The Board of Trustees met in regular session on Sunday, May 3.

Meetings of the Assembly

The Assembly met on Friday, Saturday, and Sunday, May 1, 2, and 3.

STEVEN S. SHARFSTEIN, M.D.
Secretary, American Psychiatric Association

THE AMERICAN JOURNAL OF PSYCHIATRY

Editorial

Defining the Future in Medical Education

In its report (1), the Robert Wood Johnson Foundation's Commission on Medical Education has called for a shift in medical education to a degree that calls to mind the impact of the Flexner Report of 1910, which highlighted the importance of basic science for medical education. The Flexner Report encouraged the establishment of strong departments, each with responsibility for discrete blocks of the curriculum.

Much has transpired since the Flexnerian revolution. Most recently, especially in the last 10–15 years, biomedical science has exploded and flourished. Simultaneously, there is a "health quake" currently embracing the delivery and financing of health care. The Robert Wood Johnson Commission has set forth a blueprint for the education of physicians that takes cognizance of these fast-moving developments.

Psychiatry and behavioral science, which in past decades have had varying importance in the curriculum depending on the medical school, play an important role in the Robert Wood Johnson scheme, although they are integrated into the general education of physicians.

In fact, integration is a central concept in the Robert Wood Johnson template. The commission recognizes that overly sharp boundaries between some disciplines lead to teaching that is at variance with the increasing convergence, for example, of the basic sciences. Also, the commission report recognizes the need to teach "clinical problems in the context of advances in the basic sciences." The commission encourages teaching that emphasizes how we think and the interrelations among what we know rather than artificially compartmentalized knowledge.

The lessons taught by liaison psychiatrists and by professionals in the other behavioral disciplines have influenced the core of what the commission envisions for an acceptable medical education. One of the six recommendations in the report is for physicians to have "understanding of the behavioral and social aspects of health and disease." The report takes note of the fact that maladaptive behavior plays a major role in many illnesses and that behavior change is critical to health promotion and disease prevention. The commission views as untenable the dichotomy between psychosocial and biological factors in illness.

The report also calls for 1) an expansion in training settings to ambulatory care, nursing homes, hospices, etc., 2) evaluation that matches the educational goals of the faculty and is much more derivative of faculty consideration than a function of outside test making, and 3) establishment of an appropriate and well-positioned authority that oversees curriculum change and the quality of the medical education experience.

The report deals with many other aspects of medical education, including the emotional and moral fitness of medical students, the role of modern "informatics" in the learning process, clinical epidemiology, the need to make better use of the fourth year, and the importance of the process of learning for a lifetime career rather than simply preparation for specialty selection.

Clearly, the physicians of the future will face different customs of practice. They will be equipped with much more knowledge than those practicing today. Less autonomy, more accountability, lower incomes for some, more organized health care systems, more oversight, and more team involvement are all likely to characterize the

lives of the physicians of the 1990s and beyond. The commission suggests changes in education that will equip physicians to handle these challenges and to feel satisfaction that what they learn is consistent with the challenges of practice.

Central to the commission's report is the hope that physicians, in working as partners with better informed patients, will see their role not only as prescribers of the best therapeutic advice but also as professionals dedicated to doing all they can to bring about the best possible state of health and function for the patient. The doctor, it is hoped, will not be simply a Nobel laureate in conveying knowledge but also a model partner and advocate for the patient's and family's health and welfare.

Psychiatry has an important role in helping to make students observers of their own socialization into the profession. We should help foster the development of an attitude of caretaking and responsibility for the individual in the context of family, community, and population. This will involve more focus on observation by students of their mentors' and their own behavior as they learn to become physicians who are advocates for the patient, a goal of medical education that should be given more attention.

The Robert Wood Johnson Commission has set out a lofty intent. Simultaneously, the foundation has funded eight medical schools to implement models of such curriculum change.

Psychiatry, which often has lamented its role as outsider, may take satisfaction in the fact that many of its teachings are part of a central core of curriculum reform in this report. This is good news not only for psychiatrists but also for patients because it should lead to the emergence of a more sensitive, more responsive, and more comprehensively trained physician.

REFERENCE

1. Marston RQ, Jones RM (eds): Commission on Medical Education: The Sciences of Medical Practice: Medical Education in Transition. Princeton, NJ, Robert Wood Johnson Foundation, July 1992

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The Cost-Effectiveness of Psychotherapy: A Plan for Research

Janice L. Krupnick, Ph.D., and Harold Alan Pincus, M.D.

The authors assess gaps in the current knowledge base on psychotherapy research and the cost-effectiveness of psychotherapy. Despite the considerable and increasingly sophisticated body of research on the efficacy of psychotherapy, there is an alarming paucity of studies focusing on the cost-effectiveness of psychotherapy. This problem is particularly evident in the absence of studies exploring nonclinical effects of treatment and the broader range of domains in which intervention may have an impact. Initiation of research on the cost-effectiveness of psychotherapy is important for ensuring good clinical practice and data-based policy formulation. What is needed is greater specificity regarding the populations and problems for which psychotherapy can provide the greatest benefits, identification of the variables, measures, and methodological approaches that are most useful in yielding these important data, and comprehensive quantification of the costs and effects of psychotherapy.

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The drive to contain health care costs makes critical the need to assess the efficacy and cost-effectiveness of various medical practices. In the case of psychotherapy, a sizable literature attests to its safety and efficacy (1-9), and, as demonstrated by the design of the increasingly imitated National Institute of Mental Health (NIMH) Treatment of Depression Collaborative Research Program (7), the present state of the art in psychotherapy evaluation has reached a high degree of sophistication. Little attention has been paid, however, to cost-effectiveness, particularly with reference to the broader range of societal effects.

The paucity of data in this area is puzzling given the

current economic climate and need for careful allocation of scarce resources. As the APA Task Force on Psychosocial Treatment Research observed, accountability in the practice of mental health care has been increasingly demanded by governmental bodies (J. Docherty, personal communication). If adequate research data are not provided, mental health services will be extremely vulnerable to additional budgetary constraints.

In drawing conclusions about alcohol abuse treatments, the Institute of Medicine (10) asserted that the present cost-effectiveness data are insufficient for unambiguous policy guidance, and Holder and Hallen (11) advised consideration of comparative cost-effectiveness in all investigations of treatment efficacy. Given the gaps in our current knowledge about the cost-effectiveness of treatments across the broader range of psychiatric disorders, these recommendations could be extended to any study investigating the impact of psychotherapy. The purpose of this paper is to emphasize the need to investigate the cost-effectiveness of psychotherapy, including the nonclinical effects of treatment, which frequently have been overlooked in previous studies. Our aim is to stimulate high-quality research in this area that might serve as a guide to clinical practice while providing the basis for informed policy and reimbursement decisions.

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ECONOMIC COSTS OF PSYCHIATRIC DISABILITY

Both the prevalence and economic costs of psychiatric disability are enormous: in 1988 psychiatric illnesses affected almost one-third of the U.S. adult population, who fulfilled lifetime criteria for at least one alcohol, drug abuse, or other mental disorder (12), for an annual cost of approximately \$273 billion in 1988 dollars (13). In addition to the emotional pain and suffering caused by these disorders, they are major causes of nonpsychiatric illness, disability, and death in the United States, leading to the use of costly medical resources, major losses in productivity, motor vehicle accidents, and incarceration.

Severe psychiatric impairments account for 14%–20% of work disabilities in the United States, and 11% of the people receiving Supplemental Security Income or Social Security Disability Income (SSDI) have been judged mentally disabled (14). The annual cost of depression to our society was estimated in 1986 as approximately \$16.3 billion (15), while the annual cost of alcohol and drug abuse, described recently as posing a major threat to worker health and corporate profits, is \$134.1 billion (13).

It is also known that psychological stress frequently becomes manifest as nonpsychiatric conditions requiring costly workups and treatment. Epidemiologic studies show that patients with psychiatric disturbances often seek treatment at primary care sites for medically unexplained symptoms, make at least twice as many health care visits as comparison subjects (16), and experience longer hospitalizations, incurring greater costs than patients without psychiatric comorbidity (17). This is particularly evident among the elderly, who account for a disproportionate share of health care expenditures (18). Other studies show an average prevalence of major nonpsychiatric illness of 47% among psychiatric patients and death rates that are higher than for comparison subjects. Stone and Short (19) found that nearly one of every four informal caregivers must alter work hours or take unpaid leave to accommodate care for a disabled elder and behavioral problems are most responsible for the conflict between employment and caregiving.

Finding that 75% of the costs of depression can be attributed not to direct treatment but to lost social and economic productivity, Stoudemire et al. (15) stated that timely and appropriate treatment of patients would lead to substantial savings to society. Data suggest that various substance abuse programs are also cost-effective (20), although the findings are qualified by a paucity of cost-effectiveness studies and the absence of controlled trials. As Gerstein and Lewin (20) noted, since the benefits of treatment accrue to families, neighborhoods, and businesses, it is appropriate for the public, government, and business sectors to be concerned with providing treatment and assessing its efficacy.

COVERAGE OF PSYCHIATRIC SERVICES

Insurers and federal decision makers have been reluctant to cover psychiatric services, and American com-

panies, convinced that psychiatric costs represent "the single highest cost escalation" factor among health benefit offerings (21), increasingly have separated mental health and substance abuse benefits from other health coverage.

Despite this trend, recent findings (22) suggest that the increase in costs for most psychiatric services lags behind increases for nonpsychiatric medical care. Furthermore, S. Sharfstein (personal communication) believes that coverage might be modified if researchers could convincingly demonstrate the value of psychotherapy. He has observed, for example, that German national health insurance initially excluded coverage for psychotherapy but reinstated it when researchers demonstrated a reduction in medical costs associated with psychiatric intervention. Clearly, the process by which insurers, corporations, and the federal government make decisions about coverage is complex and multifactorial, and even with substantial, valid empirical data, success is not assured. Nonetheless, in the present policy environment, it is virtually impossible even to enter the decision-making arena without such data.

GLOSSARY

Any study on the cost-effectiveness of psychotherapy needs to operationalize terms such as "psychotherapy" and "cost-effectiveness." The APA Committee on the Practice of Psychotherapy (W. Sledge, personal communication) defined psychotherapy as "a method of treating mental disorders, the cornerstone of which is the development of experiential understanding of the meaning of symptoms and/or . . . those characteristic patterns that cause the patient to suffer limitations and pain. In contrast to somatic or pharmacological intervention, psychotherapy relies on verbal means and techniques to modify characteristic ways of thinking, feeling, and behaving that interfere with the patient's capacity for maximal functioning."

Cost-effectiveness analysis has been defined (23) as a technique that compares the costs and effects of a particular program or intervention in cases where the costs and effects are expressed with different measures. Costs are usually assigned a monetary value, but effects are often expressed in other units. This approach enables readers to make up their own minds as to whether the effects achieved by an intervention warrant its cost. This approach differs from cost-benefit analysis, which also compares the cost of interventions and resultant effects but expresses all costs and effects in the same units, usually monetary. Generally, two types of costs are examined in an economic assessment of a treatment: 1) direct costs, defined (13) as the actual dollar expenditures related to the illness or disorder, which include amounts spent for hospitalization, services of physicians and other medical professionals, drugs, appliances, and rehabilitation; and 2) indirect costs, defined (13) as the value of the productivity lost because of illness, disability, or injury. This includes the value of lost

work days and housekeeping days and lowered productivity due to illness or disability and losses due to premature death.

DESIGN ISSUES

Methodologically sound cost-effectiveness studies should use the same criteria as well-designed investigations of treatment efficacy (14). In emphasizing the need for studies that broadly assess the cost-effectiveness of psychotherapy across a full range of domains of potential effects, we encourage assessment of clinical, economic, personal, and societal change, including consideration of at least the following variables.

Population

While diagnostic homogeneity and well-specified study groups are part of any methodologically sound investigation, there is disagreement as to the most productive specific population to study. Should study subjects be persons with the more common psychiatric disorders, such as major depressive disorder, panic disorder, and agoraphobia, or groups that are the most costly to society in monetary and/or social terms?

For example, there is evidence that family therapy may be cost-effective for patients with schizophrenia, a population that is extremely costly in terms of hospital charges, family burden, and SSDI payments. Spencer et al. (24) found that female patients in a poorly functioning schizophrenic group who received family therapy did significantly better in general role functioning than patients who did not have this treatment, while Falloon et al. (25) found that family therapy combined with pharmacotherapy reduced the rate of relapse and length of hospital stay in schizophrenic patients whose families had high levels of expressed emotion.

Psychotherapeutic treatment for individuals with alcohol abuse has been shown to reduce the use of medical care, sick time, and time lost from work because of injuries (26), and opiate-dependent patients who received psychotherapy had significantly more or larger gains than those who received only drug counseling (27).

Another population of interest is caregivers, e.g., for the severely mentally ill or individuals with dementia. Data reported by Brodaty and Gresham (28) show that intensive intervention for the caretakers of patients with dementia can reduce the psychological morbidity of the caregiver and delay placement of the patient in a costly institution without increasing the use of health services by either patient or caregiver.

Despite clinical biases against psychotherapy for older persons (29), studies indicate not only the efficacy but also the cost-effectiveness of psychotherapy with older adults. Thompson et al. (30), in their investigation of psychotherapies for the depressed elderly, found this group to be an underserved population that could be helped by psychotherapeutic intervention. Furthermore, Mumford et al. (31) found that adults over the

age of 55 had a greater reduction in medical service utilization after mental health treatment than younger adults, and Morisky et al. (32) reported that education and support for patients' hypertension had a more positive influence on compliance among the elderly than among younger patients.

Another potential focus is individuals who seek non-psychiatric medical treatment, since there is evidence that psychotherapy can serve as a cost-benefit adjunct to treatments of these conditions. For example, Jacobson et al. (33) observed a decrease in hospital admissions for patients with diabetes who had participated in a family-oriented teaching program. Furthermore, as demonstrated in the Rand Medical Outcomes Study (34), there is a high rate of concurrent mental disorders in persons with general medical illnesses, which might interfere with compliance and morale in efforts to treat the medical illness. On the basis of the available information, it is reasonable to assume that adding psychotherapy in a targeted way to the overall medical treatment package could improve the efficacy of the other treatment approaches and reduce disability.

Another issue is whether to focus on axis I or axis II disorders. When investigators rely on symptom-based formulations, patient clusters include those who are symptomatically similar but may be quite different on a number of dimensions that relate more to social functioning, e.g., level of developmental maturation, presence or absence of a personality disorder. Some experts (e.g., M. Horowitz, J. Docherty, personal communications) suggest that a population which might be important to study is individuals with more severe character pathology, e.g., those in the narcissistic to borderline personality range, who are often high users of psychiatric benefits.

Type of Psychotherapy

The type of psychotherapy assessed should depend on the population selected for treatment. For patients with schizophrenia, the data suggest that family treatment, including behavioral components such as problem solving and goal attainment, may be useful. Behavioral therapy, which was found to be useful and cost-effective in a clinical trial of phobic subjects and persons with obsessive-compulsive disorder (35), has also been used in the treatment of alcoholism. Matching individuals with alcohol problems to particular treatments seems to increase the average effectiveness of therapy (10), but no cost-effectiveness data are available.

Treatment packages combining psychotherapy and medication, e.g., interpersonal psychotherapy and antidepressants for depressive disorders (36) or family therapy and antipsychotic medication for schizophrenia, are obvious candidates for study. Treatment approaches such as these not only reflect common clinical practice but also provide an opportunity to study the potential interactive effects of combined therapies.

A serious difficulty in interpreting the results of many studies is the lack of specificity in describing the treat-

ments used. What is actually practiced when a particular treatment approach is used may vary considerably across practitioners, and this variation discourages reimbursement. The extent to which a treatment method can be described and operationalized contributes to the degree to which it can be standardized. The advent of manual-guided treatments and the use of audiotapes and videotapes, which can be reviewed by experts, help in clarifying whether the prescribed treatment is actually being practiced, an important advance in assessing whether a particular type of treatment is clinically potent and cost-effective for a particular type of disorder. It should be noted, however, that even the use of a manual does not guarantee the skill with which the therapy is practiced. Further standardization of treatment procedures and additional clarification of what to do when and with whom would advance the field by making the treatments more testable and identifying more clearly what has actually been done in psychotherapy.

Recent studies of clinically depressed patients have compared dynamic or interpersonal therapies with cognitive, behavioral, or cognitive-behavioral treatments. The advantages of these therapies are that they are commonly practiced, that interpersonal therapy and cognitive-behavioral therapy were specially developed to treat depression, and that these last two treatments are carefully described in detailed manuals, which facilitate assessment of the degree to which the therapist adheres to the prescribed method. It has been argued (37) that standardized treatments based on psychiatric diagnoses are conceptually incompatible with currently practiced models of psychotherapy. Also, these methods have been assessed in only a limited number of contexts, and it is unclear how generalizable such techniques may be to psychiatrically disturbed patients in nonpsychiatric settings (38). In spite of these caveats, however, we feel that the use of standardized techniques and methods, especially when adherence and competency are assessed, is a major advance in enabling researchers to more clearly determine which types of treatments work for given categories of patients.

It should be noted that some types of psychotherapy, by their very nature, lend themselves more easily than others to systematic investigation. For example, it may be easier to document change in behavior therapy, where progress can be charted on the basis of observable behavior, than in psychoanalysis or psychoanalytically derived psychotherapy. We are not suggesting that such treatments should not be studied but are simply pointing out that, given existing measures, it may be more difficult to find significant effects in investigations of some treatments than in others.

Length of Treatment

The optimal length of treatment for particular patient groups in terms of both efficacy and cost-effectiveness remains to be determined. One review of alcoholism treatments (10) suggested that, when indiscriminantly applied, interventions with more than brief durations

may have little additional benefit. In contrast, Andrews and Harvey's meta-analysis of 81 studies of core mental disorders (39) indicated that increased duration of therapy is associated with greater efficiency. The additional costs of longer-term treatment remain virtually unanalyzed, however, and there has been no examination of whether these costs are exceeded by benefits. Perhaps we need to better assess what changes take longer to achieve and whether those changes are worth the increments in resources involved in longer-term treatments. We also need to further distinguish the disorders for which longer-term therapy would be cost-effective.

Although the study of longer-term treatments adds considerable complexity and may involve a greater expenditure of research dollars, the available research data demonstrate not only that the study of longer-term work is feasible but also the importance of this issue, since the most costly mental disorders are chronic or recurrent. For example, in the treatment of patients with schizophrenia, Hogarty et al. (4) found that although good treatment effects were achieved with psychosocial interventions during 2 years of treatment, relapse rates rose rapidly when treatment stopped. On the basis of their data, these researchers recommended using strategies that could sustain compliance with maintenance psychosocial programs and pharmacotherapy over time. In their study on the role of the therapeutic alliance in the treatment of schizophrenia, Frank and Gunderson (40) found that patients who formed good alliances with their therapists achieved better outcomes after 2 years with less medication than patients who failed to establish good alliances, but the development of a therapeutic alliance was difficult and usually took at least 6 months to achieve. They noted that the patients who remained in their study groups made substantial gains; the longer they stayed, the more gains they made.

In depression research it has become clear that relapse is common after the termination of psychopharmacological or psychotherapeutic intervention. Addressing this problem in a 3-year randomized maintenance trial of patients with recurrent depression, Frank et al. (5) found that monthly sessions of interpersonal therapy could lengthen the time between episodes of depression. In a maintenance study of bulimic patients who responded to initial treatment, Pyle et al. (41) also documented a high (30%) relapse rate during the 6 months after initial treatment was completed. On the basis of a meta-analysis of the length of treatment and patient benefit, Howard et al. (42) concluded that it takes at least 26 sessions for the majority of patients to show some improvement from psychotherapy. They suggested that, on average, the maximum percentage improvement takes approximately 52 weekly sessions, depending on the patient's particular characteristics—some patients require fewer sessions and some require more.

Despite clinical assertions that greater therapy frequency leads to greater efficacy, there has also been little research on the benefit of more frequent psychother-

apy sessions (43). It would be useful to determine empirically whether greater therapy frequency leads to better clinical, and more cost-effective, outcomes than do less frequent sessions and whether there are particular disorders for which more frequent sessions are required to produce the desired results.

Type of Clinician

Research data (44) and clinical experience show that some therapists have more successful outcomes than others; for instance, trained psychotherapists achieve more successful results than primary care physicians who provide routine medical care (35), and more experienced therapists do better than novices (45). Since therapists with the most extensive training and experience are usually the most expensive, however, the question arises of what type of therapist with what degree of posttraining experience is most cost-effective.

McLellan et al. (46) found that the therapist's ability to 1) form a helping alliance and 2) adhere to the therapeutic technique are important determinants of effectiveness. Yet it is not clear whether these skills result from preexisting interpersonal strengths or clinical training. The ability to identify and interpret transference issues is more common in more highly skilled and experienced clinicians. However, how much training and clinical experience are necessary to offset the additional direct costs of the services of more senior therapists?

There is a clear movement in the field to develop competency criteria in order to assess a therapist's capacity to participate in treatment studies (47, 48). Methods have been developed and used to assess competency in various treatments and therapists' ability to adhere to the guidelines of a particular approach (48-50). Since these methods and measures are in their infancy, however, it would be useful to obtain data from additional studies at different sites to further assess the amount of additional instruction necessary to train even experienced clinicians in a specific method and to delineate the safeguards that need to be built in to ensure that therapists are adhering to the prescribed techniques.

Although investigators could reduce the costs of their studies by relying on psychiatric residents or graduate students to provide treatment, results from studies using inexperienced clinicians may not have as much impact. It is generally assumed that for the best test of a procedure, it needs to be applied by someone who is schooled and experienced in its application. For this reason, certain levels of postgraduate training and experience are considered essentials in the selection of competent therapists. These also should be people who are well-versed and experienced in the particular treatment method they will apply and who have confidence in the efficacy of their method. The advantages of using experienced therapists have been demonstrated in the review by Rounsaville et al. (48) of findings from manual-guided training programs in interpersonal therapy, which showed that experienced therapists who had been trained in dynamic therapy were able to achieve a

high level of competency in interpersonal therapy after comparatively brief training and were able to maintain adherence to the manual over the course of a long study.

Treatment Context

Although inpatient treatment is expensive and the need for hospitalization is often used as an indicator of poor outcome (27), hospitals may be the most effective setting for certain populations. Whether inpatient or outpatient therapy is more cost-effective may depend to a considerable extent on the nature of the patient population studied. For example, in a prospective study of 40 inpatients with borderline personality disorder, Tucker et al. (51) found that after 6 to 24 months of hospitalization, patients experienced a marked decline in self-destructive behavior and a significant improvement in family relationships. In contrast, Stein and Test (52, 53) found that use of a community-based program instead of hospitalization enhanced patient adjustment and produced substantial savings for a group of chronic patients, most of whom were suffering from schizophrenia.

For the treatment of alcoholism, some individuals may fare better in residential programs than in outpatient settings, namely, those with less social stability and those with dysfunctional family or work relationships (54). Other studies (26), however, show that outpatient or day treatment settings offer treatment that is at least as good as, if not better than, the treatment offered in inpatient or residential settings.

Another question is whether some patients are more effectively served in general medical settings, as opposed to specialty psychiatric settings, given the finding from recent epidemiologic studies (16) that most patients with mental illness are seen exclusively in primary care sites. There are, however, questions about the quality of care currently received by patients with mental disorder in the primary care sector (55, 56). While situating a study at a primary care site may facilitate assessment of the degree to which psychiatric intervention can affect overall health care utilization, it would be important to control for such variables as the nature and quality of care and the particular characteristics of the study group. For example, Blackburn et al. (57) noted differences in the effects of cognitive therapy and pharmacotherapy between hospital outpatient clinics and general practice clinics, and they observed that different patient populations sought treatment at the different sites.

With the growth and expansion of employee assistance programs, the work setting increasingly has been seen as an appropriate place for mental health intervention. Employees who are unable or unwilling to take time off from work to consult mental health professionals may be willing to seek out or accept services in the workplace. Because of the ease of workplace services, employees may seek help earlier in problem development, so this locale may be a potential resource for pre-

vention. Treatment at work sites may permit collection of important data regarding links between psychotherapy and effects on work.

A wide variety of treatment settings offer different treatment packages. Should one approach be, as H. Schlesinger (personal communication) has suggested, comparison of different treatment packages in different settings to determine which is most cost-effective? In addition, there is the issue of extricating specific treatments from an overall "package" provided in a particular setting, e.g., "inpatient care," although this is not a problem if the focus of assessment is the package.

Outcome Measures

An important task in designing a study on the cost-effectiveness of psychotherapy is identification of the outcomes of greatest interest and the measures that could most sensitively assess these variables. Appropriate and adequate evaluation of what may be derived by a course of psychotherapy is of particular concern given the problems of third-party reimbursers with claims for certain forms of psychotherapy (58). A third area of concern is the identification of methods by which to assign monetary values to the various outcomes.

The multiple spheres of interest in psychotherapy outcomes can generally be situated within two main categories: clinical outcomes and functional outcomes. Clinical outcomes deal primarily with psychiatric and physiological signs and symptoms and can be assessed by using symptom measures and/or assessments of general health care use. Functional outcomes pertain to changes in social role functioning as a result of psychotherapy. Some areas of interest regarding functioning in the workplace might be absenteeism (i.e., number of sick and injury days), worker turnover, job loss, productivity, earnings, and morale. Functioning as a student might involve class attendance, grades, and graduation. Marital satisfaction questionnaires and rates of marital separation and divorce might measure conjugal behavior.

It is important to assess not only the patient who has received psychotherapy but also the people whom that individual influences. For example, how the individual is functioning as a parent might be reflected in how the person's offspring are functioning personally, socially, and academically. The level of caretaking and productivity of family members also could be assessed. Other areas of concern might be the degree to which the individual is contributing to or drawing resources from the community. What involvement has the person had with social service agencies and the legal system before and after psychotherapy? What has been the nature and extent of social service and legal involvement? Has the individual been able to provide emotionally and financially for spouse, children, and/or ill or aging parents? Have child care or institutional services been used because of psychological disabilities? What measures might most efficiently help collect these data?

The final step in cost-benefit research is the translation of clinical and functional data into economic terms.

The issues here include how to assess the losses to an organization caused, for example, by absenteeism or psychiatric disability. What methods are most appropriate for assigning a monetary value to social costs, such as the cost to a community of dropping out of school, teenage pregnancy, or poor parenting? How can measures designed to assess clinical and functional behaviors be adapted to economic calibration?

Among questions to consider in this domain are the following: Do we have adequate measures for assessing social costs and are the existing measures sensitive enough to address the less tangible aspects of social functioning? Would it be useful to encourage development and refinement of methods that would enable investigators to measure more effectively the more psychologically subtle and yet important dimensions of outcome in economic terms?

Work Productivity, Creativity, and Satisfaction

In a literature review on the effects of psychiatric treatments on work restoration, Mintz et al. (14) concluded that "although there is a vast literature on psychiatric treatments, relatively little is known about the specific effects of treatments for specified conditions on the functional capacity to work" (p. 2). This view was supported by Riejhaber and Goldbeck (59), who noted that although ignored emotional problems are exceedingly costly in terms of medical utilization and a plethora of other consequences ranging from absenteeism and lowered productivity to vandalism and violence, employee assistance managers have failed to keep cost data for their mental health programs separate from their total health cost information.

Some attempts have been made, however, to assess the efficacy and cost-effectiveness of employee assistance or emotional health programs within organizations. These do not represent methodologically sound, controlled investigations, but they provide promising exploratory data. For example, 60% of employees who received up to 10 sessions of insight-oriented or cognitive-behavioral therapy through an emotional health program at Equitable Life Assurance Society (60) said that the services they received were very helpful in terms of the presenting problem and job attendance, performance, and satisfaction. For employees with stress-related disorders, for every dollar invested in the program there was a \$5.52 return on that investment in terms of increased productivity per person per year, although it was not clear how these figures were calculated.

In a study of the effects of mental health intervention on 12 out of 37 alcoholic employees who were enrolled in a Kennecott Copper Corporation program for an average of 1 year (61), the absentee rate decreased by 50%, sickness and accident costs decreased from \$70.67 to \$25.33 per month, and medical/surgical costs decreased from \$109.04 to \$59.91 per month. The employees who were categorized as alcoholic but did not receive treatment worsened in all categories.

In an American Telephone and Telegraph employee as-

sistance program providing crisis intervention (62), 86% of the treated subjects were considered "rehabilitated" or "improved" after treatment; rehabilitation was defined as "restoration to a former state of health and efficiency." In terms of job performance, before treatment 76% were rated poor, 17% were rated fair, 7% were rated good, and 0% were considered excellent; after treatment, 79% were rated as good or excellent and 36% were rated excellent. Comparison of 22-month periods before and after treatment showed that days of absence were reduced from 421 to 92, and occasions for absence declined from 172 to 35. There was a significant reduction in disability absences, from 1,531 days of disability before treatment to 192 days after treatment. Of 44 employees referred to the employee assistance program who were in known job jeopardy, 40 retained their jobs, saving the company \$84,000 in job training for new employees.

Although the association between psychotherapy for troubled employees and increased attendance, and perhaps increased productivity, has been made in these studies, the studies themselves are highly problematic because of severe limitations in study design. There is a notable lack of specificity in delineating who the subjects were, what disorders they suffered from, what the treatments were, who administered them, and for how long and in what context they were received. Also, since many of these reports were published by the companies that offered the services, the degree of investigator bias is unclear.

Moreover, it is not clear that appropriate measures of work productivity, creativity, and satisfaction exist. The work subscale of the Social Adjustment Scale and the Quality of Well-Being Scale may be two useful assessments in this domain, but they do not seem adequate for the entire task because it is important to ascertain not only the individual subject's assessment of his or her own productivity and creativity on the job but also assessments by other key figures, such as employers or supervisors. Furthermore, do we have adequate operational definitions of such constructs as "productivity" and "creativity"? Are there measures of functioning in these domains? Of the measures that do exist, can they provide assessments from different perspectives? It would not be difficult to construct a job satisfaction scale, but would this provide information on capacity, productivity, and creativity? Furthermore, is it possible to translate greater work effort and increased ingenuity (if these are assets to the business) into monetary value? Work restoration is not the only aspect of work functioning with financial implications. Which specific aspects of work should be included in a cost-effectiveness assessment of psychotherapy? Should aspects such as the quality of job performance be included, and if so, is there a valid and reliable way to make judgments in this area?

Ability to Attend School or Graduate

School attendance and completion are similar in many respects to work restoration and functioning. At

the lowest level of quantification are the simple issues of whether a student attends classes and graduates. More subtle issues are attitudes toward schooling, school adjustment, functioning, and morale. What are the direct and indirect costs of dropping out of school? Whose school adjustment should be assessed—only individuals who receive treatment or also family members, whose ability to attend and function in school may be affected by a patient? What is the relationship between school failure and other social problems, such as crime, substance abuse, teenage pregnancy, and reliance on Aid to Families With Dependent Children? On an even more subtle level, is there a way to quantify the cost to society of an individual's failure to maximize his or her educational potential?

Ability to Care for Family

If psychotherapy is successful, one would expect its recipients to gain an increased capacity to nurture others functionally, financially, and psychologically. If it increases the ability to secure and maintain employment, financial strains on the family should be reduced. If it helps to keep a parent out of the hospital, the costs of child care are eliminated or reduced. If it increases the capacity of a caretaker to keep a mentally ill family member in the home because of a greater ability to handle stress, the costs of institutionalization may be reduced. Some questions here may be related to how one operationalizes a concept such as "ability to care for the family." Should this be based strictly on the capacity of the individual to provide food and lodging for dependents, without requiring outside help to do so, or can qualitative judgments involving the quality of care also be included? Can this be expressed in monetary terms?

Marital Satisfaction

There is evidence that psychotherapy can produce improvements in family functioning and adaptive coping (63), but there are no data regarding the monetary cost of marital dissolution and the degree to which psychotherapy might reduce those costs. S. Sharfstein (cited in reference 64) reported a sixfold increase in medical utilization in the year following marital breakup, although S. Budman et al. (unpublished 1980 paper), comparing groups of individuals who received group therapy versus no therapy after marital separation, found that the experimental subjects were less distressed after treatment but did not utilize health care services significantly less. However, detecting offsets in medical costs in areas where there is already a rich provision of services is difficult. Furthermore, what are the costs of family disintegration beyond medical utilization? It has been shown (65) that the income of divorced women and children falls substantially in the years following a divorce. Does this translate into a greater need for social services? What are the increases in legal fees and court costs for settlement disputes and custody battles? What is the cost of psychiatric services

for spouses and children who are traumatized by the disruption and the parents' diminished capacity to nurture their children in the years following divorce (66)?

Health Care Costs and Utilization

The primary focus of cost-effectiveness research on psychotherapy has been the impact on health care utilization. A number of studies have confirmed the economic advantage of using psychotherapeutic services, particularly in producing offsets in medical costs. For example, in a meta-analysis of 34 studies, Mumford et al. (67) found that relatively minor interventions for people who recently had suffered heart attacks or were facing surgery had large effects in speeding recovery and shortening hospital stays. Schlesinger et al. (68) showed that individuals who had at least seven sessions of psychotherapy after the diagnosis of one of four chronic diseases used 66% fewer medical services during the third year after treatment than a no-therapy group with the same diseases. In a study of myocardial infarction survivors (69), the survival rate for those who had undergone 12 months of group therapy was 10% higher than the survival rate for the no-therapy group and 19% higher when only severe cases were considered. In a review of 22 studies, Jones and Vischi (70) found a mean reduction of 34% in medical care utilization after mental health intervention and a mean reduction of 45% after participation in alcoholism programs. In three studies of health maintenance organizations (71), medical utilization rates declined for psychotherapy patients who initially had been high medical service users. Jameson et al. (72) estimated that inclusion of outpatient psychotherapy benefits reduced monthly medical costs by \$9.41 per patient.

These pioneering studies suggest the cost-effectiveness of psychotherapy and provide a solid foundation on which to build, but basing current policy decisions on them is problematic, since many were conducted more than a decade ago, before considerable advances in research methods delineating psychotherapy and improvements in diagnosis and assessment. In addition, there is now disagreement as to the best ways to assess medical utilization and the role of this variable in assessing the overall cost-effectiveness of psychotherapy. Some investigators use medical claims to assess utilization, while others feel that this approach does not assess the degree of offset with enough precision. Some investigators (e.g., H. Schlesinger, personal communication) feel that the existing work on the medical cost offset of psychotherapy is adequate and that formulations can be drawn, while others have raised questions about the utility of the approach to cost-effectiveness research used in previous studies. For example, although Levitan and Kornfeld (73) assessed the cost-effectiveness of providing a liaison psychiatrist for hip fracture patients on an orthopedic unit and showed a shorter length of stay and lower hospital costs in the liaison group than in the no-liaison group, Lyons et al. (74) argued that although the liaison group

had a shorter length of stay, no attempt was made to ensure that this did not merely indicate premature discharge. In reviewing the study by Schlesinger et al. (68) on the impact of mental health treatment on medical care utilization for patients with one of four chronic diseases, Lyons et al. (74) cited three major problems: 1) the treatment and no-treatment groups were not necessarily equal in severity of illness, 2) the effectiveness of the interventions was not studied, and 3) utilization of services is not synonymous with need for services. Given the further clarification of issues and refinements in methodological techniques that have occurred since the early studies were conducted, it seems that new investigations could add to and update existing data. The recent replication by Strain et al. (75) of Levitan and Kornfeld's hip fracture study involved major improvements in design and methodology and demonstrated important savings in medical care costs.

Given serious national concerns about current health care expenditures, the impact of psychotherapy on medical costs is certainly not an area to overlook. It is not, however, the only area of interest or importance. We are not critical of the existing literature per se but see it as too narrow in focus. Exploring cost-effectiveness exclusively in terms of the offset in medical care costs may trivialize mental disorders, and it narrowly defines the potential societal cost savings of psychiatric treatment.

Social Costs and Social Service Utilization

As discussed earlier, some of the more substantial changes that result from psychotherapy may be more in the social rather than medical realm of functioning, and yet there has been little investigation of these effects. Might psychotherapy decrease not only health care costs but also social care costs? Can it lead to a reduction in the use of social services, and if so, which ones and to what extent? Can psychotherapeutic services reduce criminal activity? If so, which could then in turn reduce police, legal, and court costs?

It is important once again to consider the effects of psychotherapy not only on the individual receiving treatment but also on family members and caregivers, whose own levels of mental health and social functioning may be seriously affected by the demands of an emotionally disabled dependent. What are the clinical and functional outcomes for caregivers when they or people who depend on them receive psychotherapeutic help? As Brodaty and Gresham (28) demonstrated, it is not only the identified patient but also the caregivers for that person who may suffer psychological morbidity because of the emotional and perhaps physical demands of their role. When caregivers "burn out," suffering psychiatric or social disability themselves, tax-supported social services often must be employed. Thus, the well-being and social efficacy of these individuals have cost implications for the rest of society. How do we measure the monetary value of the services of such individuals and the savings to the family and

society when their coping abilities are supported and sustained?

BARRIERS TO RESEARCH

In addition to the practical problems of conducting any research, two potential problems are particular to this area: identification of who would carry out this type of investigation and determination of whether the tools exist for carrying it out effectively.

Are there sufficient numbers of investigators with both the interest and competence to conduct this type of research? Would it be sufficient to create interdisciplinary teams, bringing in researchers from psychiatry, psychology, and health economics, or would it be advisable to create training opportunities, possibly in the form of postdoctoral research fellowships, to train specific individuals in the methods of conducting cost-effectiveness studies in psychotherapy and other mental health treatments?

As M. Kamlet (personal communication) has observed, measurement in this area involves some thorny issues, including the limitations of existing measures. For example, it may be possible to obtain qualitative descriptions of such domains as marital relations, friendships, and work productivity, but can these areas be measured adequately in quantitative terms? Kamlet asserts that while there exists at least one scale in this area (Kaplan's Quality of Well-Being Scale), measurement is not quantified in the way that an economist would approach it. In calibrating scores on these types of measures, economists may see numerical scales as arbitrary and the meaning of one score relative to another as unclear. Thus, there may be serious difficulties in translating psychiatric data into economic terms. Another question is whether there are adequate instruments for measuring "softer" areas of functioning, such as worker morale and the relationship between such variables as morale and productivity. Most investigators have shied away from dealing with variables that are so difficult to measure, yet focusing only on easily quantifiable variables means that a good deal of the richness of psychotherapy's benefits is overlooked.

SUMMARY AND RECOMMENDATIONS

A large body of existing data, including numerous meta-analyses of psychotherapy efficacy (1, 39) and critical findings on schizophrenia (4), depression (36), and anxiety (9), indicates that psychotherapy has substantial power to alleviate extraordinarily destructive and painful illnesses. It is becoming increasingly apparent, however, that those who advocate improved reimbursement for psychotherapy will have to make a strong case not only for its interpersonal and social benefits but also for its monetary benefit to policymakers, employers, payers, and the public. The existing data on the cost-effectiveness of psychotherapy indicate

that 1) little current research activity relates to this area; 2) previous studies have been narrow in scope, are few in number, and have had substantial methodological limitations; and 3) important design and measurement issues need to be carefully considered.

Investigations stimulated by a series of workshops sponsored by NIMH and APA (76) demonstrate that quantification in the area of cost-effectiveness of mental health services is feasible. After these research development workshops, which were aimed at stimulating outcome research in consultation-liaison psychiatry, 12 grant proposals on the cost-effectiveness of these services were submitted to NIMH for scientific review, and six of these were funded.

What is needed is greater specificity regarding the populations and problems for which psychotherapy can provide the greatest benefits. More research also is needed to identify the variables, measures, and methodological approaches that are most useful in yielding these important data. Of most concern is the paucity of studies that attempt to quantify the costs and effects of psychotherapy in a comprehensive manner, producing results which can be used by researchers, policymakers, and the public. High-priority issues include the following.

1. Advancing the state of the art in cost-effectiveness analysis (77) by developing and/or modifying methods to make it more applicable to psychotherapy and more comprehensible to policymakers in this arena.

2. Gathering and assessing existing instruments for measuring psychotherapy-related change, as Waskow and Parloff (78) did in 1975, to assist investigators and to determine whether the instruments needed to conduct this type of investigation exist.

3. Supporting methods development aimed at creating and/or refining outcome instruments for cost-effectiveness studies that include assessment of nonclinical outcomes.

4. Encouraging the routine inclusion of cost data in all psychotherapy outcome studies in order to begin to define the relative cost-effectiveness of various psychotherapy treatments for specific disorders.

5. Expanding federal and other research funding of studies aimed at discovering the costs and effectiveness (across the broad range of domains) of different treatment approaches.

6. Providing training opportunities for clinical researchers with a career interest in developing and refining methods for studying the cost-effectiveness of psychotherapy.

It is only by facilitating and supporting well-designed cost-effectiveness research that we may learn the full role that psychotherapy can play in reducing human suffering and the long-term social and economic costs of mental illness.

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Panic Disorder in Children and Adolescents: A Review

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***Objective:** Panic disorder has been considered an adulthood disorder that does not occur in children or adolescents. The authors' goals were to critically review the available evidence for panic attacks and/or panic disorder in children and adolescents, to review the limited data on the biological basis of panic disorder as it has been studied in children and adolescents, to discuss the possible treatment approaches for panic disorder in children, and to suggest potential opportunities for further research on panic disorder in children. **Data Collection:** Sixty-three articles pertaining to panic disorder in children and adolescents were critically reviewed. These articles included retrospective histories of adults with panic disorder, clinical case reports of children and adolescents with panic disorder, studies of psychiatrically referred children and adolescents, reports from epidemiologic community and school samples of children and adolescents, studies of children and adolescents at risk for psychiatric disorder, reports of panic-like symptoms in pediatric patients, family studies of panic, studies of the biological basis of panic in adults, and studies of treatment for panic. **Findings:** There is strong evidence that panic disorder occurs in children and adolescents and that its clinical presentation in this population is similar to that found in adults. **Conclusions:** Extending the many adult studies of panic disorder to children and adolescents would be extremely fruitful. Like adults with panic disorder, many children and adolescents are brought to emergency and medical clinics for the physical symptoms of unrecognized panic disorder.*

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Although anxiety symptoms are common in children of all ages and both sexes (1), only three anxiety disorders (overanxious disorder, separation anxiety disorder, and avoidant disorder) are classified specifically as disorders of childhood. Family studies and retrospective reports of childhood symptoms by adults with anxiety disorders suggest a continuity between childhood and adult anxiety disorders. Early childhood histories of separation anxiety disorders in adults with panic disorder have been reported (2). Other studies have linked an early history of separation anxiety disorder to several other adult anxiety disorders such as generalized anxiety disorder and agoraphobia (3, 4) as well as a predisposition to other types of psychopathology (3). Panic disorder, however, has been considered a disorder of adulthood that does not occur in children or adolescents. There is now evidence sup-

porting the occurrence of childhood panic attacks with symptoms that are qualitatively distinct from those of separation anxiety disorder.

Isolated panic attacks occur in about 10% of adults, and recurrent panic attacks not meeting full diagnostic criteria occur in about 3.6% of adults (5). The rate of full-blown panic disorder is smaller (1.6%). There is increasing evidence that panic attacks and panic disorder are seriously disabling conditions with high morbidity (6-8). Moreover, a childhood onset of these disorders may be especially impairing. A report from the National Institute of Mental Health (NIMH) Epidemiologic Catchment Area (ECA) study (8) indicated that panic disorder with first onset at age 17 or younger was associated with greater risk of alcohol abuse, suicidal thoughts, suicide attempts, and use of emergency rooms than onset at age 18 or older.

Several retrospective reports from adults of their age at onset of panic attacks (9-12) have appeared, suggesting that panic attacks begin in childhood. However, before 1987 there were no published cases of panic attacks or panic disorder based on direct studies of children. In 1987, Casat et al. (13) reported the case of a 12-year-old girl with separation anxiety disorder and mitral valve prolapse. The girl reported symptoms suggestive of adult panic disorder, including tachycardia, sweating, dyspnea, generalized weakness, and "butter-

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flies" in her stomach accompanied by school refusal. She later developed fears of crowds, heights, strangers, and being alone. Casat et al. suggested that some children with separation anxiety disorder may develop agoraphobia and panic attacks in adulthood. In 1989, three separate reports of panic attacks and/or panic disorder in a total of 24 children appeared (14-16).

In addition to retrospective reports of adults with panic disorder and clinical case reports of children and adolescents with panic, further evidence that panic attacks and/or panic disorder occur in children and adolescents can be found in clinical case reports of treatment of panic in children and adolescents, in assessments of psychiatrically referred children and adolescents based on structured diagnostic interviews and *DSM-III* criteria, in reports from epidemiologic community and school samples of children and adolescents, in studies of children and adolescents at risk for psychiatric disorders by virtue of their parents' psychiatric disorder, and in reports of panic-like symptoms in children and adolescents seen in pediatric services.

The purposes of this paper are 1) to critically review the available evidence for panic attacks and/or panic disorder in children and adolescents, 2) to review the limited data on the biological basis of panic disorder as it has been studied in children and adolescents, 3) to discuss the possible treatment approaches for panic disorder in this population, and, finally, 4) to suggest potential opportunities for further research on panic disorder in children and adolescents.

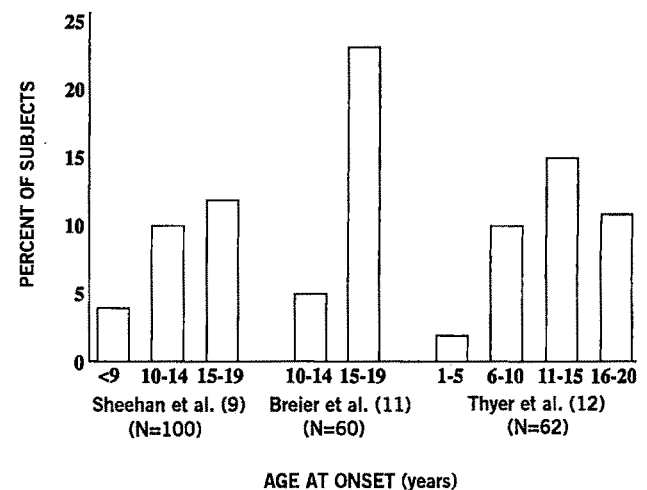
REVIEW OF THE LITERATURE

Retrospective Reports of Adults With Panic Disorder

In several studies of adults with panic disorder (9-12), the subjects retrospectively reported that their panic disorder began in childhood or early adolescence (figure 1). These reports have received little attention. Sheehan et al. (9) studied 100 patients 19-61 years old who had *DSM-III* panic disorder with agoraphobia. The range of age at onset of panic was 5-58 years; the mean age at onset was 24.1 years. Twenty-six patients reported experiencing symptoms before the age of 20 years: 12 were between 15 and 19 years old, 10 were between 10 and 14 years old, and four were younger than 9 years old. Of interest and concern is the fact that the mean time from onset of symptoms to treatment for the total sample was 12.7 years.

Breier et al. (11) reported on age at onset of panic disorder in 60 adults with agoraphobia, mixed phobia, and/or panic disorder diagnosed according to Research Diagnostic Criteria (RDC). Seventeen (28%) of these patients reported that their panic disorder began before they were 20 years old. Eleven patients (18% of the sample) reported that their first panic attack occurred between the ages of 10 and 17, three (5%) reported that their first panic attack was at age 18, and another three (5%) reported that their first attack was at age 19.

FIGURE 1. Retrospective Reports of Age at Childhood Onset of Panic



On the basis of a retrospective chart review of 62 adults with *DSM-III* panic disorder without agoraphobia whose mean age at onset was 26.6 years (range=5-51), Thyer et al. (12) reported that 38% of the patients experienced symptoms before the age of 20 and 11% experienced symptoms before the age of 10. Thyer et al. obtained similar results in 95 adult patients diagnosed with panic disorder and agoraphobia.

The NIMH ECA study (17), which included a probability sample of more than 18,000 subjects 18 years old and older living in five U.S. communities, found a peak onset of panic disorder between the ages of 15 and 19. More than 18% of the adults in this study reported experiencing panic before they were 10 years old, and an additional 7% reported experiencing panic between the ages of 10 and 15.

Klein et al. (18) reexamined their data on childhood panic attacks and panic disorder in two study groups: 343 consecutive admissions to an adult anxiety disorders clinic and 560 first-degree relatives of patients admitted to an anxiety disorders clinic. Using the data from structured diagnostic interviews administered by trained clinicians, they determined that nine (1%) of the 904 subjects reported experiencing spontaneous panic attacks before they were 13 years old. Klein et al. reviewed the narrative summaries of these nine subjects and concluded that only three of them gave reports consistent with four-symptom spontaneous panic attacks occurring in childhood. They pointed out the inherent problems in the validity of retrospective reports of panic and suggested that the definition of spontaneous panic "is best done in the context of a series of such attacks."

Although these reports suggest that panic disorder occurs in children and adolescents, retrospective reports of their childhood by adults are subject to problems of recall such as distortion and revision in addition to the validity issue raised by Klein et al. (18). In addition, prepubertal status at the time of onset of panic in

TABLE 1. Case Reports of Panic Disorder in Children and Adolescents

Study	Year	Subjects With Panic Disorder	Age Range (years)		Subjects With Coexisting Disorders	
			At Time of Report	At Onset	Separation Anxiety	Mitral Valve Prolapse
Vitiello et al. (19)	1987	2	8-10	1-5	2	1
Biederman (20)	1987	3	8-11	4-8	1	—
Ballenger et al. (14)	1989	3	8-13	—	—	1
Black and Robbins (21)	1990	6	14-28	4-15	3	—
Vitiello et al. (22)	1990	6	8-12	5-11	4	2
Black et al. (23)	1990	2	8-12	8-9	1	—

the subjects who retrospectively reported childhood onset was not established in these studies. Therefore, direct assessment of children and adolescents with panic disorder is critical to further our understanding of this disorder in this population.

Case Reports of Children and Adolescents

There are case reports of panic disorder in 22 children and adolescents that support adults' retrospective reports of their age at onset of panic disorder (14, 19-23) (table 1). Because many children with panic come from families with panic, the recognition of the child's disorder may represent a selection bias because parents with panic disorder may be more likely to recognize the symptoms in their children. Even though most of these studies did not use a structured diagnostic interview and cannot provide rates because of sampling problems, they are of interest because the diagnoses were made by experienced clinicians who provided details of the clinical phenomena.

These preliminary reports provide directions for future research based on sound methodology: use of structured diagnostic interviews, direct interviews with the child and the parent, and assessment of referred as well as nonreferred populations.

Vitiello et al. (19) made the first such report in a letter to the editor in 1987. They diagnosed *DSM-III* panic disorder in two prepubertal boys, one inpatient and one outpatient, using a structured diagnostic interview. The boys had been referred for separation anxiety. Their symptoms included shortness of breath, palpitations, chest pain, paresthesia, and trembling. Both boys had developed agoraphobia and school refusal. A family history of panic disorder was found in both children.

Biederman (20) reported panic disorder in three prepubertal children, two boys and one girl. Symptoms included restlessness, muscle tension, palpitations, sweating, and dry mouth in one boy; multiple autonomic symptoms in the girl; and symptoms of fear and shaking in the other boy. Two of the children refused to attend school, and the mothers of two of the children had a history of agoraphobia. Clonazepam was used successfully in all three children to reduce anxiety, and the children's functioning returned to normal.

Ballenger et al. (14) reported on three children, two girls and one boy, who had *DSM-III* panic disorder with ago-

raphobia, all of whom responded to alprazolam and imipramine. Symptom complexes varied for each child but included dizziness, tingling, trembling, shortness of breath, palpitations, and a cold and clammy feeling. A family history of panic was reported in one child.

Black and Robbins (21) described six adolescents with panic disorder, two boys and four girls. Only one of these adolescents reported prepubertal onset of panic disorder. Symptoms included hyperventilation, flushing, sweating, shortness of breath, dizziness, tachycardia, and paresthesia in most of the subjects and isolated symptoms of shaking, headaches, faintness, and palpitations in all of the subjects. All six subjects reported a history of depression. A family history of panic disorder with agoraphobia was reported in one adolescent. Four of the children responded favorably to desipramine or imipramine.

Vitiello et al. (22) also reported *DSM-III-R* panic disorder in six prepubertal children, five boys and one girl, referred to an academic child psychiatry service. All but one of the children were outpatients. All of these children had heart pounding, weakness, trembling or shaking, and feelings of dying or going crazy. Five children had shortness of breath, lightheadedness or dizziness, and chest tightness or pain. Four children had tingling of fingers or face, feelings of choking or smothering, and sweating. None of the children reported hot or cold flashes or blurred vision. School avoidance was diagnosed in three of the children. The diagnoses of separation anxiety disorder and school avoidance were independent of panic disorder. The mean interval between first panic attack and diagnosis was 3 years. A family history of panic disorder was found in all six children.

In a letter to the editor, Black et al. (23) reported on two additional prepubertal girls with panic disorder and agoraphobia. The diagnosis in both children was based on a structured diagnostic interview of the child and the parent. The 8-year-old girl had mild depressive symptoms and developed separation anxiety disorder subsequent to her panic disorder. Her father had a history of panic disorder with agoraphobia. She described sudden onset of fear accompanied by sweating, a "funny feeling in my throat," a "funny smell," trembling, nausea, feeling hot, her "heart feeling funny," and fear of loss of control. The 12-year-old girl reported onset of panic at age 9. Her attacks were char-

TABLE 2. Reports of Panic Disorder in Psychiatrically Referred Children and Adolescents

Study	Year	Sample	N	%	Subjects With Panic			Subjects With Coexisting Separation Anxiety	
					Age Range (years)		Boy:Girl Ratio	N	%
					At Time of Report	At Onset			
Alessi et al. (24)	1987	61 inpatients	10	16	14-17	12-15	4:6	4	40
Alessi and Magen (25)	1988	136 inpatients	7	5	7-12	3-12	4:3	6	86
Last and Strauss (26)	1989	177 outpatients	17	10	14-18	9-18	6:1	2	12

acterized by "sudden onset of extreme fearfulness, crying, breathlessness, dizziness, flushing, sweating, tachycardia, palpitations, tremulousness, feeling that she may lose control, nausea, headache, feeling a lump in the throat, and pleading with her parents to take her away from whatever situation they were in." There was no significant morbidity or family history of anxiety disorder. Both children were reported to respond favorably to tricyclic therapy. Despite the presence of a "funny smell" in the list of symptoms for one of these children, the authors did not consider the possibility of temporal lobe epilepsy. However, this girl's positive response to tricyclic therapy favors the diagnosis of panic.

Although these reports are of interest because of their clear clinical descriptions of panic in children, they suffer from sample bias and lack of structured or semistructured diagnostic interviews. In addition, in the absence of data from placebo-controlled trials, these reports of treatment efficacy must be considered tentative.

Assessment of Psychiatrically Referred Children and Adolescents

Diagnoses of panic disorder have been made in studies of psychiatrically referred children and adolescents using the Schedule for Affective Disorders and Schizophrenia—Childhood Version and *DSM-III* criteria (24-26) (table 2). The subjects were referred for psychiatric treatment for multiple reasons, not necessarily panic symptoms, and thus provide some limited data on the frequency of panic in psychiatrically referred children and adolescents.

Alessi et al. (24) found that 10 of 61 adolescents on an adolescent psychiatric inpatient unit had panic disorder according to RDC and that another 15 had possible panic disorder. All but one of the 10 patients with definite panic disorder had a comorbid depressive disorder. The mean age at onset of panic was 13.9 years, and no prepubertal onsets were reported. More than half of the adolescents with definite panic disorder reported symptoms of sweating, trembling, palpitations, and feelings of faintness. Trembling was reported by nine of the adolescents with panic disorder.

Alessi and Magen (25) diagnosed panic disorder in seven of 136 children consecutively admitted to a child diagnostic and research inpatient unit. Four of the chil-

dren with panic disorder were boys and three were girls. The most common referral symptoms were school refusal and aggression, followed by depression and somatic complaints. Trembling or shaking, dyspnea, palpitations, and dizziness were reported by five of the children with panic disorder, and chest pain, choking, faintness, fear of dying, hot and cold flashes, and sweating were reported by three. Paresthesias were reported in one child. Depressive disorders were diagnosed in four of the children.

Last and Strauss (26) reported that 10% of 177 consecutive referrals to an outpatient pediatric anxiety clinic had *DSM-III-R* panic disorder. Only one prepubertal child had panic attacks, and only one adolescent reported a prepubertal onset of panic. Panic symptoms resembled those found in the adult disorder. Palpitations/tachycardia, trembling, and flushes or chills were each reported in 94% of the patients with panic disorder, shortness of breath and sweating by 82% and dizziness/faintness by 75%. All other panic attack symptoms, except choking, were present in more than half of the children with panic disorder. Comorbidity was found in approximately half of the children, most commonly another anxiety disorder. Of interest is the fact that 33% of the mothers met *DSM-III-R* criteria for a lifetime diagnosis of panic disorder.

Again, the issue of prepubertal status was not specifically addressed in these studies. The age range of the children and adolescents (7-18 years), however, suggests that at least some of these children were prepubertal at the time of their panic.

Epidemiologic Community and School Surveys of Children and Adolescents

There have been no large, multisite epidemiologic surveys of children and adolescents using current psychiatric diagnostic criteria comparable to the ECA data on adults. Three small epidemiologic studies have reported on panic disorder (16, 27, 28) (table 3).

Hayward et al. (16) reported that the lifetime prevalence rate of at least one four-symptom panic attack in 95 ninth-grade students whose mean age was 14.5 years was almost 12%. Eight girls and three boys had panic disorder. Three other boys reported limited symptom panic attacks.

TABLE 3. Epidemiologic Surveys of Panic in Children and Adolescents

Study	Year	Sample	Instrument	Subjects With Panic	
				N	%
Hayward et al. (16)	1989	95 ninth graders	Structured Clinical Interview for DSM-III-R Disorders, panic disorder section	11	11.6
Macaulay and Kleinknecht (27)	1989	660 children in the community	Panic Attack Questionnaire	88	13.3
Whitaker et al. (28)	1990	356 high school students	Columbia Clinics Interview	2	0.6

Macaulay and Kleinknecht (27) surveyed 660 children and adolescents 13–18 years old. They found severe panic with symptoms similar to adult panic disorder in 30 of the subjects and moderate panic in 58 of the subjects. Severe panic included symptoms of distress and seriousness, but moderate panic referred to either distress or seriousness. There was no significant difference in frequency of attacks between subjects with severe and moderate panic. Girls outnumbered boys by about three to one. The median age at onset of panic was 13 years.

In a two-stage epidemiologic survey of a New Jersey community, Whitaker et al. (28) initially screened 5,000 students 14–17 years old for multiple psychiatric symptoms, including panic symptoms. During the second stage of the study, 356 students were interviewed with a semistructured interview yielding *DSM-III* diagnoses. The interviews were conducted by individuals who were blind to the results of the first stage of the study. A diagnosis of panic disorder was made on the basis of results from the Columbia Clinical Interview (29). The lifetime prevalence rate of panic disorder reported—0.6%—is similar to that reported in persons with onset at age 17 or younger in the ECA. Fewer than half of the students with panic disorder in the study of Whitaker et al. had received treatment for their symptoms.

The Whitaker et al. study used semistructured interviews, albeit before the development of validated semistructured *DSM-III* interview protocols suitable for use with children and adolescents. The other two studies used self-report questionnaires, and only Hayward et al. (16) had the diagnosis confirmed by a child psychiatrist using *DSM-III-R* criteria. *DSM-III-R* criteria were used to make a diagnosis of panic attacks, but the frequency of attacks was not reported so the diagnosis of panic disorder could not be confirmed. Despite these limitations, these data clearly support the occurrence of panic attacks in children and adolescents and support the high probability of such attacks meeting *DSM-III-R* criteria for panic disorder.

Studies of Children and Adolescents at Risk for Psychiatric Disorder

We reported on the occurrence of panic disorder in children at risk for psychiatric disorder by virtue of depression in one or more parents (15). Six (2.7%) of the 220 children in this study met *DSM-III* criteria for

panic disorder. A seventh child, who was 9 years old, reported panic attacks that did not meet the frequency criteria for *DSM-III* panic disorder. Diagnoses were made by a child psychiatrist and were based on all available information, including structured diagnostic interview of child and mother. The range in age at onset of panic disorder in this study was 5–18 years. Two of the six children with panic disorder were clearly prepubertal (they were 5 and 6 years old) at onset of panic. The prepubertal status at onset of panic of three of the children, who were 10, 12, and 13 years old, was not determined. Comorbid illnesses were common among the six children, particularly major depression and separation anxiety disorder. The symptom pattern of the panic attacks resembled that of the adult disorder. All six children reported shortness of breath, and five children reported palpitations. Chest pain, choking, dizziness, sweating, trembling, fear of death, faintness, and feelings of unreality were found in three of the children. Two children experienced tingling, and one child described hot and cold flashes. The parents of four of the children had panic disorder in addition to major depression.

Reports of Panic-Like Symptoms in Children and Adolescents Seen in Pediatric Services

Children with depressive disorders have been shown to have frequent somatic complaints (30, 31). Although there are many reports in the literature on childhood hyperventilation, the relationship of hyperventilation to panic attacks is unknown (32). Four studies in the pediatric medical literature (33–36) suggest the occurrence of panic attacks in children and adolescents (table 4).

Herman et al. (33) examined Mayo Clinic records over a 25-year period and found 34 children diagnosed with hyperventilation syndrome whose symptoms were suggestive of panic attacks. When these children were contacted for follow-up information, many reported chronic anxiety. van Winter and Stickler (34) reported panic disorder in six children at the Mayo Clinic. Herskowitz (35) reported on four children with panic attacks who were brought to pediatric services with neurological symptoms.

In a retrospective chart review of all cases seen between 1984 and 1988 by the psychiatric consultation-liaison service at a tertiary referral pediatric hospital, Garland and Smith (36) diagnosed four cases of *DSM-*

TABLE 4. Reports of Panic-Like Symptoms in Children and Adolescents Seen in Pediatric Services

Study	Year	Study	Subjects With Panic-Like Symptoms	Age Range at Onset (years)	Diagnosis
Herman et al. (33)	1981	Retrospective chart review of clinic patients	34	6-18	Hyperventilation syndrome
van Winter and Stickler (34)	1984	Case reports of clinic patients	6	9-17	Panic disorder
Herskowitz (35)	1986	Case reports of clinic patients	4	9-16	Panic attacks
Garland and Smith (36)	1990	Retrospective chart review of hospital patients	4	8-15	Panic disorder

III-R panic disorder. Three children were referred to psychiatry after months of medical workups yielding no organic etiology for somatic complaints. Substantial complications in the children's school and family functioning were noted. The authors suggested that children with the somatic complaints of panic disorder may be brought to pediatric services. If confirmed, this would be comparable to the situation for adults with panic disorder, who often seek medical rather than psychiatric treatment (37).

The Nature of Panic in Children and Adolescents

Some investigators question whether the nature of panic is similar in children and adults. Acute, sudden onset of physiological symptoms and the attribution of such sensations to losing control or going crazy seem to be necessary for a diagnosis of panic attacks. Nelles and Barlow (32), on the basis of Piaget's theory of cognitive development, expressed doubts as to whether children have the cognitive capacity to make such an attribution. The studies reviewed here (13-16, 18-28, 34-36) suggest that children experience the same physiological symptoms of panic as adults and also, like adults, attach fearful or catastrophic significance to these physical sensations. These fears and physical sensations do not seem to be invariably associated with or brought on by separation from a major attachment figure. Therefore, they appear to be distinct from separation anxiety disorder, which, in any event, is characterized by somatic complaints, not physiological symptoms suggestive of autonomic hyperactivity. Further detailed clinical study of the symptom pattern of children with panic disorder is needed.

Family Studies of Panic

Several studies have examined rates of anxiety disorders in the relatives of adults with anxiety disorder (38-41). Other studies have examined the rates of these illnesses in the relatives of children with anxiety disorders (42). A review of these and other studies in progress supports the familial nature of panic disorder (43).

To our knowledge, only one study has reported on the rates of anxiety disorders in the relatives of children with a diagnosis of *DSM-III-R* panic disorder. Last et al. (44) compared the rates of anxiety disorders in the first- and second-degree relatives of children 5-18 years old who had anxiety disorders (including panic disorder)

with rates of anxiety disorders in the first- and second-degree relatives of children who had attention deficit disorder and were never psychiatrically ill. Diagnoses of anxiety disorders were made in 94 children on the basis of results obtained from the Schedule for Affective Disorders and Schizophrenia for School-Age Children (KIDDISADS) (modified for *DSM-III-R*) administered to the child and the parent. Adult relatives of 94 children with anxiety disorders, nine of whom had a primary diagnosis of panic disorder, were given the Structured Clinical Interview for *DSM-III-R* and the childhood disorders sections (separation anxiety disorder, overanxious disorder, attention deficit disorder, avoidant disorder) of the modified KIDDISADS. The child relatives of the children with anxiety disorders were given the complete modified KIDDISADS. First-degree relatives of children with anxiety disorders had higher rates of anxiety disorder than first-degree relatives of two control groups. More specifically, the relatives of children with overanxious disorder had higher rates of panic disorder than the relatives of children with separation anxiety disorder and other anxiety disorders. There was a trend for relatives of children with panic disorder to have higher rates of panic disorder than relatives of children with other anxiety disorders. The small number of family studies that included children limit conclusions and suggest a potentially interesting area for further research.

DATA ON THE BIOLOGICAL BASIS OF PANIC IN CHILDREN AND ADOLESCENTS

There have been considerable research efforts in adults to identify potential biological markers for panic. Catecholamine levels, frequency of mitral valve prolapse, and agents that produce laboratory models of panic attacks have been studied. The latter include lactate infusion, carbon dioxide inhalation, isoproterenol hydrochloride, yohimbine hydrochloride, and caffeine, which can produce panic attacks in laboratory subjects with a history of panic disorder. These invasive challenge tests are used in research studies exploring the biological differences among anxiety disorders and the physiological basis of panic attacks (45). Therefore, their use in children for research purposes has been necessarily limited.

There has been some suggestion of an association between mitral valve prolapse and panic attacks in adults.

Both disorders can present with similar symptoms mediated by hyperactivity of the autonomic nervous system. The diagnosis of mitral valve prolapse is made by cardiac auscultation, which reveals a characteristic mid- to late-systolic click and/or late systolic murmur, and by echocardiogram. The prevalence of mitral valve prolapse in the general population is 3% to 4% (46). Women are more commonly affected than men. Age appears to affect the prevalence of mitral valve prolapse; children have rates of 1% and adolescents show rates approaching those found in adults (46). Mitral valve prolapse diagnosed by echocardiogram has been associated with panic disorder in adults in several studies (47–50) but not in others (51–53).

The literature on a possible association between mitral valve prolapse and anxiety in children is sparse. In a study of 813 children 9–14 years old, Arkfen et al. (54) found that the prevalence of mitral valve prolapse diagnosed by cardiac auscultation was 4.2%. These authors found no difference in anxiety scores between a group of children with mitral valve prolapse and a group of children without mitral valve prolapse. In an unpublished study Gorman and Klein (personal communication) found that mitral valve prolapse was diagnosed by echocardiogram in three out of 16 children with anxiety disorders, the majority of whom had separation anxiety disorder. The possible co-occurrence of mitral valve prolapse and panic disorder in children warrants further exploration based on these findings. We are currently conducting such a study at our institution.

Only one published study has examined biological markers in children at risk for panic disorder by virtue of panic disorder in their parents (55). Thirty-nine children, 7–17 years old, were examined for mitral valve prolapse by cardiac auscultation and echocardiogram, lactate levels after maximal exercise, 24-hour urinary catecholamine levels, and platelet monoamine oxidase (MAO) activity. Although a trend toward higher 24-hour catecholamine levels and greater MAO activity were found in the high-risk children than in normal control subjects, there were no statistically significant differences between children of patients with panic disorder and normal control subjects on any of the tests.

TREATMENT FOR PANIC ATTACKS: BEHAVIORAL AND PHARMACOLOGICAL APPROACHES

Behavioral and cognitive therapy as well as pharmacotherapy have been systematically tested in adults but not in children or adolescents with panic disorder. Clinical trials in adults have shown that exposure (56) and medications such as tricyclic antidepressants (57), fluoxetine (58), alprazolam (59), lorazepam (60), and clonazepam (61) are effective in reducing the symptoms of panic. The use of cognitive and behavioral treatment in children with anxiety, particularly fears and phobias, has been reported in open trials and clinical practice (62), but there are no controlled clinical trials of these

treatments with children. Pharmacological studies in children with anxiety disorders in general have been extremely limited and include neuroleptics, psychostimulants, antihistamines, and anxiety and antidepressant medications. The data so far are inclusive and limited. Therefore, there is no scientific basis yet to support the use of these medications in children with anxiety disorders, with the possible exceptions of tricyclic antidepressants for separation anxiety disorder and obsessive-compulsive disorder (63). Pharmacological treatments that are efficacious in adults with panic disorder have been used in clinical practice for children with panic (14, 20, 21), but clinical trials are absent.

IMPLICATIONS FOR FUTURE RESEARCH AND CASE FINDING

Our review suggests a number of potential directions for future research on panic attacks and/or panic disorder in children and adolescents. Information that is emerging from the studies of adults with panic disorder could fruitfully be extended. This could include studies of the natural history and clinical course of children whose panic disorder and symptoms were systematically diagnosed and assessed and who were followed longitudinally, family-genetic studies of children with panic to attempt to replicate the familial aggregation findings found in adults, studies of the biological markers of panic in children, and controlled clinical trials of behavioral and pharmacological approaches for the treatment of panic in children.

Thorough diagnostic evaluations using structured diagnostic interviews and *DSM-III-R* criteria could be conducted in children with panic disorder. These children could be followed longitudinally to determine the evolution of symptoms as well as the natural history and course of childhood-onset panic disorder. Do children with panic disorder continue to have panic when they reach adulthood?

Biological studies that have proved fruitful in adult patients with panic and that pose no psychological or physical threat to the child (examples include echocardiograms and determining catecholamine levels) could be conducted to determine the prevalence of mitral valve prolapse in children with panic disorder and in children with other anxiety disorders or with no anxiety disorders. Do children with panic have higher mean 24-hour catecholamine levels than children with other anxiety disorders or children with no anxiety disorders?

Finally, research methods and designs used to study behavior therapy and pharmacological therapy in adult patients with panic disorder could be applied to the study of children with panic disorder. It would be important to compare differences and similarities among children, adolescents, and adults with panic disorders to determine if and how age affects treatment response.

In terms of case finding, children with panic disorder, like adults with the disorder, probably are brought to emergency and medical clinics for physical symptoms

(i.e., hyperventilation, dizziness, palpitations), and their diagnosis may go unrecognized. Therefore, pediatric and neurology clinics and pediatric emergency rooms may be important areas for case finding. In addition, there is reasonable evidence that children of parents with panic and anxiety disorders are at greater risk for having panic, so some of the cases may be found in these families.

Our review suggests that panic disorder occurs in adolescents and, less frequently, in prepubertal children. The field is ripe for a host of studies developed in adults to be extended to children. These studies must, of course, take into account the special needs of and precautions for this younger age group.

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Clinical Problem Solving and the Biopsychosocial Model

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Engel's biopsychosocial model, while unifying the sciences relevant to medicine under general systems theory, is of limited utility in organizing bedside clinical problem solving. The authors consider this issue in light of the structure and goals of the clinical encounter. The biopsychosocial model is a model for organizing the sciences relevant to medicine; however, medical/psychiatric practice poses problems both within and outside the scientific realm. Since the biopsychosocial model cannot account for clinical problems to which the methods of science do not apply, the authors seek to facilitate biopsychosocial problem solving by proposing a clinical decision-making model that complements the biopsychosocial model. Their model directs the clinician's attention to three core aspects of the clinical encounter: problems of knowledge, ethics, and pragmatics. The authors reconsider Engel's case of Mr. Glover to demonstrate the anticipatory emphasis of the model. Other clinical examples are used to demonstrate the difficulties arising from mistaking one kind of aspect of medicine for another. When these three aspects of medicine are respected equally, a biopsychosocial practice is unavoidable.

(Am J Psychiatry 1992; 149:1315-1323)

The biopsychosocial model of medicine and psychiatry (1, 2) is an influential paradigm in psychiatry (3), family practice (4), and research (particularly psychiatric research) (5). It provides models for treatment by emphasizing the multidimensional nature of medical problems and demonstrating the functional interdependence of these multiple dimensions. Yet, to what degree does the biopsychosocial model actually shape clinical decisions? Concerns are frequently voiced about its lack of utility in everyday clinical decision making (6-9), its inability to differentiate important from unimportant clinical data (7, 8), and the tendency for it to be used in understanding clinical situations retrospectively rather than prospectively (7, 8). One empirical study (10) demonstrated that medical students prefer to use biomedical rather than biopsychosocial conceptions of illness, and another study (11) verified this trend among clinicians treating mood disorders. Psychiatrists are no exception to this tendency to have difficulty in using the biopsychosocial model. Paul Fink, in his response to an APA presidential address (6), noted that the everyday applicability of the model is a critical problem for psychiatry. Indeed, Fink raised the possibility of "biopsychosocial" being but an empty catchword with little methodological bite.

The biopsychosocial model was intended to preserve scientific rigor while attending to the whole person. The model is based on general systems theory, in which the sciences are organized around a systems hierarchy (2, 12). The systems hierarchy is organized around levels of organization, the lowest of which is subatomic particles, and there is a progression up through higher levels such as the molecule, cell, organ, person, couple, community, and biosphere. Each system level is interdependent with the others, and none has functional priority over the others, at least in theory. This model was and is much needed, given the reductionism of the biomedical model that characterizes much practice and research (1, 13). The systems hierarchy provides a means for conceptualizing the often-observed dependence among biological, psychological, and social levels of organization.

Why has the biopsychosocial model had limited success in changing physicians' behavior in actual clinical problem solving? That is, why are physicians not *practicing* biopsychosocial medicine? There is surely a multiplicity of reasons: physicians vary in their time constraints, in their interest in nontechnical (or nonprocedural) aspects of patient care, and in their sources of professional satisfaction. Many of these preferences may be incompatible with practicing truly biopsychosocial medicine. There are also conceptual reasons for the biopsychosocial model's limited assistance in clinical problem solving. This article focuses on those reasons.

Two key conceptual problems shape the difficulties in using the biopsychosocial model (i.e., practicing biopsychosocial decision making). The first has to do with the systems hierarchy itself. The systems hierarchy is

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not hierarchical: it provides no functional priority of one level over another (14), at least as far as clinical problem solving goes. The clinician-user has no guided priorities to structure clinical decisions. Thus, the clinician has no method for determining which system level is most critical to the problem at hand. The second conceptual problem has to do with the way the biopsychosocial model is conceived as a medical model. We will show that it methodologically limits the scope of medical inquiry in ways that are antithetical to Engel's (and biopsychosocial practitioners') intent.

First, however, let us review Engel's conception of the biopsychosocial model. According to Engel, the model is a scientific one: "In any consideration of a scientific model for medicine that would qualify as a successor to the biomedical model, be it the biopsychosocial or any other, the fundamental issue is whether physicians can in their study and care of patients be scientists and work scientifically in the human domain" (15, p. 113). The admirable thrust of Engel's lifework has been to open up all areas of medical life to scientific inquiry. Engel endorses this definition of science from Charles Odegaard: "Science represents man's most persistent effort to extend and organize knowledge by reasoned efforts that ultimately depend on evidence that can be consensually validated" (15, p. 115). For Engel, then, a medical model should be scientific, and for it to be scientific, its knowledge claims must be supported by reasons and evidence that are open to consensual validation. However, is scientific inquiry relevant to all problems that arise in the clinical encounter? The answer is no, if one considers ethical and practical problems a part of medical/psychiatric practice. Indeed, the methods of science, we will show, are very well-suited to establishing knowledge about areas relevant to medicine but are methodologically ill-suited to other problems in clinical practice. As the examples below illustrate, many significant clinical problems in medicine defy resolution with the methods of science alone. In his later work, Engel himself increasingly views the biopsychosocial model as a model for the scientific *aspects* of medicine, rather than a general medical model (15). The bulk of this article demonstrates the importance of ethical and practical problems to biopsychosocial decision making and proposes a simple complement to the biopsychosocial model that provides a biopsychosocial problem-solving method.

THE STRUCTURE OF THE CLINICAL ENCOUNTER

Before going further, we need to define some fundamental concepts that are relevant to the tasks of any medical model. First, what is the context or situation in which the goals of medicine are realized? Fundamentally, these goals are realized in the clinical encounter—the clinical relationship between the physician and the patient. Medical research, public health, and so forth play supportive roles when the *practice* of medicine is considered.

The various sorts of events that transpire in a doctor-patient relationship are what we call the clinical content. Because the clinical encounter is conducted over time, the clinical content changes over time. Examples of clinical content could include taking a psychiatric history, performing a physical examination, performing a gastric lavage, discussing a treatment compliance problem with a cocaine addict, or making a psychotherapeutic interpretation. In the course of the clinical encounter, the clinician attends to some things and ignores others. The clinician's attention is selective, and the object of attention is thematic for that moment. The theme of the encounter is the clinical content that the physician selects at a particular point. A particular kind of clinical theme is the clinical problem (16). Clinical problems are nodal themes in the clinical encounter, since they often provoke changes in the clinician's inquiries or prompt the clinician to take therapeutic action. Examples of clinical problems could include determining the diagnosis of schizophrenia, evaluating the role of cholecystokinin in cholelithiasis, managing blood loss in a gunshot victim, improving a patient's compliance with an antihypertensive medication regimen, or deciding whether to fund treatment for the homeless mentally ill rather than prenatal care for the medically indigent. Clinical problems reflect the broad diversity of difficulties in rendering health care.

The clinical problem is the fundamental unit of decision making in the clinical encounter (16). Indeed, a focus on clinical problems (instead of disease entities) has already established itself in psychiatric record keeping (17–20). The idea that clinical problems are the fundamental unit of medical decision making is quite different from the usual idea that a diagnosis, disease, or illness is the fundamental unit. However, considering the actual decisions a clinician makes in everyday work will make this point obvious.

Consider this fictionalized example of a clinician's activities today. Perhaps he came into the office at 8:00 a.m. and found a statement from an insurance company that is supposed to be paying for his treatment of an adolescent with borderline personality disorder. The company says his treatment was unnecessary and it will not pay. Perhaps he had a 9:00 a.m. patient that he could not see until 9:40. Now the patient is very angry. He might wonder how to deal with the patient's anger. Or perhaps he consulted with the family of a patient in the intensive care unit whose intracranial hemorrhage has left her in a coma for 11 days. He might wonder when to begin discussing discontinuation of treatment with her family.

The point in these examples is that the clinician's decision-making process is not limited to diagnostic/treatment considerations at all; instead, it focuses on the everyday problems that clinical work presents. Moreover, clinical problems are not limited to explaining biological factors, understanding behaviors or meanings, or integrating these data. Nevertheless, these activities encompass the task of scientific medicine as

Engel conceives it. Our examples here and later illustrate that scientific understanding is only a part of the larger task of taking clinical action. A medical model that embraces only scientific understandings will not address important clinical problems.

How can we conceptualize a clinical method that will answer the complete range of clinical tasks? On the basis of Pellegrino's analysis of the clinical encounter (21-23), we propose three types of clinical content and, derivatively, three types of clinical problems. These three "faces" of medicine embrace a biopsychosocial approach and provide the means for addressing the special categories of clinical problems we have mentioned. The three faces or aspects are the epistemic aspect, the ethical aspect, and the pragmatic aspect.

The Three Faces of Medicine

Epistemic aspect. This aspect of medicine concerns much of the scientific or empirical basis of the clinical encounter. The epistemic aspect has to do with clinical knowing. When considering the contribution of basic and clinical science to clinical decision making, one is probably considering the epistemic aspect of medicine. For example, the epistemic aspects of medicine could include conceptualizing and testing a diagnostic classification system for psychiatric disorders, making a clinical diagnosis, choosing a treatment based on studies of clinical efficacy, or choosing the best approach in counseling a stubborn patient. The epistemic aspects pertain to understanding or explaining clinical events.

Ethical aspect. This aspect includes factors in the clinical encounter related to choosing preferable (in the evaluative sense) courses of action. Ethical aspects of medicine could include decisions about risk/benefit ratios for treatments, the justification for withholding important treatment information from a patient, or decisions about distributing scarce treatment resources, such as intensive care beds. The ethical aspects of medicine deal with values, and ethical problems have to do with 1) value conflicts between doctor, patient, and relevant others, such as nurses, families, and society, and 2) threats to valued things or values themselves, such as a diabetic patient's loss of a leg and subsequent loss of independence. The ethical aspect forces clinical decisions based not on science alone but on values as well (24). This is one reason why the biopsychosocial model, as currently formulated, is of limited assistance in dealing with this category of clinical problem: the biopsychosocial model is a narrowly defined medical model with science as its core method. How can a method for the attainment of knowledge resolve problems involving a clash of values?

Pragmatic aspect. This aspect pertains to translating clinical knowledge and ethical choice into effective therapeutic action. Pragmatics pertain to what is done or what action is taken. Pragmatics are necessarily intersubjective—relevant to actual dealings with people. The pragmatic aspects will often emphasize predicting clinical events. Examples could include modifying a

drug regimen according to anticipated drug interactions, anticipating potential problems with treatment compliance in a patient of a different ethnic background, modifying office management procedures, or meeting Medicare payment guidelines. A pragmatic problem could be not knowing what to do or how to do some relevant task. A pragmatic problem may involve not having sufficient supplies, materials, or assistance, i.e., not having drugs or equipment available. Pragmatic problems prevent effective therapeutic action. The science and art of prognosis is a clinical area in which pragmatics is made concrete. Pragmatic aspects of medicine require actions based on common-sense (or other utilitarian) criteria. Thus, medical scientific knowledge, or the pursuit of it, is only a requirement of, but not the same as, pragmatic *doing*.

Three aspects of one medicine. The three aspects of medicine can be considered explicitly or implicitly in any clinical situation. That is, a clinician can apply each of these aspects to a clinical theme in greater or lesser degrees. Significant overlap from epistemic to ethical to pragmatic aspects occurs. Consider this example from consultation-liaison psychiatry. The clinician is admitting a reluctant and delirious patient to the coronary care unit. The obvious pragmatic problem is considering what to do next if the patient refuses admission. Epistemic considerations could include choosing an interviewing approach that will enhance the patient's consent to admission. At the same time, an ethical consideration could be the status of the patient's competence to choose admission, with the attendant conflict of protecting or restricting the patient's freedom. Note that these three aspects are simultaneously present in the clinical encounter, yet they are distinguishable from one another. Each aspect illuminates the clinical goals by providing a relevant context for those goals.

It may be tempting to (mis)construe our intent as merely renaming the psychosocial aspects of medicine as the ethical and pragmatic aspects of medicine. This would miss a major point of this article. The psychosocial aspects of medicine as described by Engel have to do with the scientific conceptions of the nonbiological aspects of human life: those aspects of life that are studied by scientific disciplines such as psychology, sociology, and anthropology. The ethical and pragmatic aspects reflect a much broader context of study, one that may include these sciences but also include disciplines that are not scientific at all and are perhaps more properly considered humanities. For example, solving an ethical problem may require moral philosophy, while solving a pragmatic problem may require a business management technique. Most important, ethical problems in medicine require their own method for problem solving, that of resolving competing values. Pragmatic problems require their own method for problem solving, too; that is, common sense. (Ironically, systems theory has much to offer common sense!) Both ethics and pragmatics are readily distinguishable from the knowledge-acquiring methods of science.

Advantages of Considering the Three Faces

Precisely because both biomedicine and biopsychosocial medicine are properly scientific models for the scientific part of medicine, these models fall short in accounting for the complete clinical encounter by excluding pragmatic and ethical meaning and the taking of clinical action based on those meanings. Clinical problems in these models formally focus on epistemic problems exclusively: What is the diagnosis? What is the most effective treatment? What does this symptom mean? If students and residents are trained to make inquiries about only scientific facts concerning a patient (10, 25–29), then they will ignore the ethical and practical problems that so stubbornly impede the realization of therapeutic goals. The patient is dehumanized—is functionally an object for scientific study. These students mature into practitioners who resent and avoid the ethical and practical aspects that have always been part of medical practice. When only fact gathering is emphasized to students, ethical and pragmatic problems are made a troublesome, intrusive irritant in the practice of scientific medicine.

However, by formally considering the three aspects of medicine, the clinician cannot avoid practicing biopsychosocial medicine as it was ideally intended. When the clinician seriously considers and acts upon ethical and pragmatic clinical problems (as well as epistemic ones), the biopsychosocial approach cannot be avoided or ignored. How can one solve ethical problems without considering the values, wishes, ambivalences, and personal histories of the people involved? How can a clash of values be understood without making an empathic connection? How can one solve practical problems without considering the social systems that influence the patient or without considering the psychological and social sciences? Once the epistemic, pragmatic, and ethical dimensions of the clinical encounter are considered equally, the biopsychosocial perspective is unavoidable. In considering these three faces of medicine, the biopsychosocial approach is utilized by focusing reasoning and inquiry, without reviewing every science relevant to medicine. Indeed, what drives clinical decisions is not a structural hierarchy but the moral goals of the clinical encounter (8).

What do we mean by considering the three faces? We mean simply that every clinical problem has a theme that is reflected by the three faces, as in the example of the reluctant delirious patient. One or more themes may be explicit, others implicit. In our example, admitting a reluctant patient to the hospital is a pragmatic theme. However, when we ask ourselves how to solve this problem, the overlap with the epistemic and ethical themes can emerge. How should the patient be approached? Is the patient competent?

In order to realize therapeutic goals, the clinician's decision making must provide a way of planning for, or anticipating, future clinical problems. The biomedical model anticipates future clinical (epistemic) problems through its discipline of pathology, which predicts the

longitudinal course of diseases. The biopsychosocial model of Engel recommends a diversity-of-sciences approach but provides no guidelines for selecting the science that applies to a particular patient at a particular time (7). Moreover, the biopsychosocial model provides no formal method of anticipating the idiosyncratic problems that every individual patient presents; only the interdependence of the various system levels is emphasized. The three-aspect method proposed here acknowledges the importance of scientific explanation and prediction while also accounting for the individual, unique person.

RECONSIDERATION OF THE CASE OF MR. GLOVER

In Engel's classic article "The Clinical Application of the Biopsychosocial Model" (2), the case of Mr. Glover provides an example for the application of the biopsychosocial model. We will recast this familiar case to illustrate the three faces decision-making model as well as to highlight the differences between the biomedical model, the biopsychosocial model, and the supplemented biopsychosocial model we propose.

In the original case, Mr. Glover, a driven, overly responsible man, suffers his second myocardial infarction at work. Denying to himself the seriousness of his illness, he continues working until his boss notices his visible discomfort and convinces him to go to the hospital. There he relaxes until an inept intern repeatedly fails to obtain an arterial blood sample. Unnerved and in pain, Mr. Glover begins to doubt the competence of the hospital staff, and his chest pain increases again as his anxiety mounts. He loses consciousness as ventricular fibrillation ensues. The hospital staff jump to the conclusion that he was lucky to be in the hospital when this happened, or else he would be dead. The doctors fail to realize that events that occurred in the hospital may have contributed to Mr. Glover's cardiac arrest (8).

How does the biomedical clinician interpret this case? How does the biomedical clinician decide what data are clinically meaningful or important? The biomedical model would emphasize the importance of the empirical signs and symptoms of myocardial infarction and would bring to bear action that would address the acute course of this disease, including the increased risk of fatal cardiac arrhythmias. The biological aspects of the case would be seen as therapeutically and etiologically most important, with the psychosocial aspects relegated to the background if they are considered at all.

In contrast, the biopsychosocial clinician would emphasize the interdependency of biological and psychosocial contributions to Mr. Glover's illness. In retrospect, the anxiogenic effects of the failed attempts at obtaining an arterial blood sample would be considered important to the development of arrhythmias. This is an example of how the interpersonal system level would have a direct impact on the organ and cellular levels, and vice versa. Note that precisely *how* a particular case interpretation is developed is not clear with either model.

In the case of the biopsychosocial model, the clinician is left without guidance toward anticipating and effectively intervening at the appropriate system level. Moreover, as we will describe, certain aspects of clinical reality are deemphasized by both models.

For the recasting of Mr. Glover's case, let us put ourselves in the place of the clinician in the emergency room, where the actual first meeting with Mr. Glover would occur. The physician would have no information about Mr. Glover other than what he or she could obtain firsthand. This scenario will illustrate the application of the three faces of medicine under conditions that are more reflective of a real clinical encounter. This is important, because the test of a problem-solving model is its utility in the face of uncertainty.

Let's say that Dr. Smith is now meeting Mr. Glover to examine him in the emergency room.

Smith: Hello, I'm Dr. Smith. What seems to be the trouble?

Glover: Aw, I've been having some chest pain. I don't think it's a big deal, but my boss insisted that I come in.

Smith: You've had this sort of thing before?

Glover: Yeah, I had a heart attack 6 months ago.

Smith: You've broken out into a sweat and look pretty pale. Let me get you to lie down while I have the nurse hook up an ECG. Tell me more about your heart disease.

Glover: I had a heart attack 6 months ago; since then I've only needed to take nitroglycerin occasionally. You don't think this is another heart attack, do you?

Smith: That remains to be seen, but in the meantime, we ought to keep you comfortable. How much pain are you having?

Glover: It was hurting quite a bit at work, but it's a little better now.

Smith: Any other symptoms?

Glover: I had nausea at work and felt weak.

Smith: Where does it hurt?

Glover: Here (points to substernal region) and down this (left) arm.

Smith: Just like your heart attack before?

Glover: Pretty much.

Smith (examining Glover's chest): I think there's a good chance you're having another heart attack, so I want you to take it easy for now. There will be an intern coming in to draw some blood and finish your exam, and the nurse will give you some pain medication and some Valium.

The initial clinical priority in any first-time clinical encounter is making sense of the patient's clinical complaints. This is obvious and an example of an epistemic problem, namely, understanding Mr. Glover's medical problem. Dr. Smith accepts Mr. Glover's complaint of chest pain at face value and tries to characterize it as one of the many types of chest pain he has encountered in his training and experience. In this way, he may statistically specify and predict potential events of clinical significance. Thus, this aspect of his clinical inquiry resembles a natural scientific inquiry, explanation, and prediction (30, 31).

As Dr. Smith conducts his inquiry into the chest pain, he anticipates potential new clinical problems. This anticipation of future problems is the initial priority of the pragmatic face of medicine. The tentative diagnosis of

myocardial infarction foretells a range of dangerous clinical possibilities. Dr. Smith notes the incongruity between Mr. Glover's casual dismissal of his complaint as "some chest pain" and his observable diaphoresis and pallor. Dr. Smith wonders whether Mr. Glover is denying to himself the severity of his illness. Dr. Smith sees this as an important potential pragmatic problem; if Mr. Glover is seriously ill and denies it, he may refuse lifesaving treatments. Dr. Smith keeps in mind this hypothesis of Mr. Glover's denial for later interactions with Mr. Glover.

The ethical aspects of this encounter are more implicit. The ethical priority is to ask the question, What values are at stake when I take any clinical action? Dr. Smith works in a setting—the emergency room—where the ethics are significantly different from those of other outpatient or inpatient settings. For example, Dr. Smith feels less bound to provide careful disclosure for informed consent, because such disclosures interfere with undertaking effective and potentially lifesaving therapeutic action in the limited time available. Thus, Dr. Smith has in effect decided to override the ethical demand for complete disclosure at this time. However, if Mr. Glover contests this relative lack of disclosure, the ethical aspects of the case could emerge as an ethical problem that would demand attention from Dr. Smith. Dr. Smith, then, as a biopsychosocial clinician, should attend to Mr. Glover's wishes for more information.

Glover: Valium? What for?

Smith: To help you relax so your heart won't have to work so hard.

Glover: It's not going to knock me out is it? I want to know what's going on.

Smith: Let's see how you do with the pain medicine alone, but it's important that you relax. (Dr. Smith leaves the room, and nurse Brown attends to Mr. Glover.)

Glover (to nurse): You know, I really didn't want to come in here because of my work, but now I do feel a lot better. What is this pain medicine anyway?

Brown (smiling): Morphine; it should help you feel even better.

Glover: Seems like pretty strong stuff for chest pain.

Brown: We don't want people with heart attacks to hurt. (Nurse Brown attends to various technical procedures and leaves as intern enters.)

Dr. Smith's sensitivity to a potential ethical problem is borne out by Mr. Glover's behavioral response to the offering of analgesics and anxiolytics. Mr. Glover's concern about avoiding excessive sedation and maintaining control of himself suggests to Dr. Smith the potential for power struggles with the patient. Recognizing Mr. Glover's compulsive personality style, Dr. Smith compromises a pragmatic goal, control of anxiety, in order to obviate an ethical conflict, that is, handling Mr. Glover's implicit refusal of diazepam. At the same time, Dr. Smith brings to bear a rudimentary knowledge (epistemic aspect) of the compulsive personality in shaping his choice to forgo the diazepam.

Dr. Smith, as a preceptor to his intern, now turns his attention to the encounter with Dr. Young and Mr.

Glover. Ever vigilant, he pragmatically considers what potential problems could emerge from this interaction as he moves to the next patient in the next room. He wonders whether Dr. Young's own anxiety about doctoring will somehow compound Mr. Glover's anxiety and makes a mental note to check in on them shortly.

Young: Hi, Mr. Glover. I'm Dr. Young, the intern working with Dr. Smith. I need to go over some of the information again that you discussed with Dr. Smith and do a more complete physical.

Glover (sighing): Okay. (Dr. Young takes the history and examines Mr. Glover.)

Young: Mr. Glover, I need to take an arterial blood sample from you to determine if your blood has enough oxygen. You can expect the stick to hurt some.

Glover (tensing up): Can I look?

Young: If you want. (Dr. Young attempts to draw the arterial blood but has difficulties. After Dr. Young has made several unsuccessful attempts, Dr. Smith returns, as he had planned.)

Smith: How's it going?

Young (nervously): Fine.

Glover (anxious and in pain): Can't this guy just get the blood?

Smith (diplomatically, to Dr. Young): Let's get Ms. Brown to hold his wrist while we go over another case. Mr. Glover, I don't think the arterial blood sample is essential at this time. Let's hold off on it until you're more comfortable. How's your chest pain?

Glover (relieved): Better, thanks.

Smith (looking at the ECG monitor): You got pretty excited with that stick, but you're already settling down.

Glover: You'll be back soon?

Smith: Sure. In the meantime, Ms. Brown will be with you. (Mr. Glover is taken to the coronary care unit without complications.)

When Dr. Smith reenters the room, witnessing Mr. Glover's clenched teeth and grimace, he immediately concludes that things are not going well at all, despite Dr. Young's reassurances. Effective action is needed, and Dr. Smith has a number of important pragmatic factors to consider before acting. Is Mr. Glover dyspneic enough to warrant the arterial blood gas procedure? Is the need for the procedure more important than keeping Mr. Glover calm and collected? Is it ethical to allow Dr. Young, a trainee, to continue his painful attempts to draw arterial blood when these very attempts may present some degree of risk to Mr. Glover (i.e., precipitate a cardiac arrhythmia through increased sympathetic tone)? In his deliberation, Dr. Smith keeps in mind his goal of getting Mr. Glover safely to the intensive care unit. Dr. Smith's pragmatic consideration of these ethical and epistemic factors prompts his decision to withhold further attempts at the arterial blood gas procedure, and indeed he successfully transfers Mr. Glover to the intensive care unit.

Note that in this example, the three faces (epistemic, ethical, pragmatic) are interdependent. Dr. Smith's choice to withhold diazepam (a pragmatic move) is dependent on his knowledge (epistemic aspect) of the pathophysiology of myocardial infarction, the relation-

ship of anxiety to arrhythmia, and so on. Dr. Smith's withholding of diazepam is also dependent on his view of the ethics of paternalism, that is, how he views the conflict between a patient's refusal of treatment and the need for urgent and beneficent action. Dr. Smith's priorities are tripartite: 1) (epistemic aspect) what is the problem? 2) (pragmatic aspect) what actions need to be taken and what will be their consequences? 3) (ethical aspect) what value implications do my actions have? Precisely because he moves comfortably from clinical knowledge to clinical ethics to clinical pragmatics and back again, Dr. Smith is a truly biopsychosocial clinician. Working through the three faces provided him a problem-solving map for the uncertainties of on-your-feet practice.

THE PROBLEM OF CROSSED-ASPECT DECISION MAKING

Earlier in this article we discussed briefly the training of medical students—a process dominated by the lesson that medical science is the primary discipline relevant to the practice of medicine. These students may develop into practitioners whose expectation is that all clinical problems can be solved with the well-honed tools of the natural scientific inquiry. Indeed, the overwhelming majority of material in medical school curricula is basic and clinical science. For these students (and many practitioners), there is only one face of medicine: the epistemic aspect. The most obvious difficulty with single-aspect decision making is the one that inspired Engel's "biopsychosocial" response: attending to a narrowly defined science in medicine dismisses the broad range of human experience and dehumanizes patients. We now illustrate why the single-aspect approach to clinical decision making may often be fruitless in dealing with ethical and pragmatic problems and, in some cases, may be even dangerous to patients.

We use the term "crossed-aspect" decision making to describe the situation in which a clinical problem in one face of medicine is confused with another. The confusion or misidentification can lead to great difficulty in solving a clinical problem. This confusion can be avoided simply by reconsidering the clinical problem in light of all three faces or aspects.

Examples of Crossed-Aspect Decision Making

Applying an epistemic solution to an ethical problem. A colleague discussed with one of us an ethical problem that occurred in the context of the psychiatric emergency room. He had a patient, brought in by police, who was refusing to be meaningfully interviewed. The patient had a history of violent psychotic illness, so an evaluation would be essential if there was to be any possibility of his release into the community. Our colleague's problem was whether it was ethical to tell the patient, "You should talk to me, because if you don't, I have no choice but to commit you to the hospital."

Intrigued, we pursued his thinking about this problem. His solution was to survey the emergency room psychiatrists, asking them how they handled this situation. Our colleague was quite reluctant to consider what values were at stake. Instead, he thought that if the majority of the emergency room psychiatrists did it one way, that must be the right way. In effect, our colleague was applying an epistemic solution to a correctly identified ethical problem. What is disturbing, even dangerous, is his thinking that scientific data gathering, which indicated consensual agreement only, would be sufficient to suggest right (ethical) action. Of course, in some cases it could dictate a right action or, more likely, reveal some way of avoiding or circumventing the ethical problem. Nevertheless, what was needed to answer the ethical problem was a qualitative inquiry into the competing values at stake (32). The idea that consensual agreement about practices is adequate for making ethical choices can be dangerous. In the extreme it can result, as in Nazi Germany, in consensually agreed-upon atrocities (33). Inquiries that give equal respect to the three faces moderate the extremes of any single mode of decision making.

Mistaking a pragmatic problem for an ethical one. An internist, Dr. A, consulted one of us for an "ethical" problem he had with a critically ill, elderly patient. The patient, Mr. Z, had experienced cardiac arrest, had an anoxic cerebral injury, and was diagnosed as being in a persistent vegetative state. He had a living will and had told his internist and family members that if he became a "vegetable," he would not want to be kept alive artificially. The internist had planned to withdraw life-sustaining treatments, but he had been threatened with a lawsuit by Mr. A's estranged daughter. The daughter wished "everything be done" to keep Mr. Z alive, despite her knowledge that her father preferred otherwise. Dr. A was now hesitant to discontinue treatment. Upon further questioning, Dr. A outlined his rationale for the ethical discontinuation of Mr. Z's treatment. It became clear to him, and to us, that his best ethical judgment—to discontinue treatment—was reasonable; thus, problem-solving efforts should be focused instead on the practical (pragmatic) problem posed by the daughter: litigation. The case was resolved by bringing in the hospital attorney to discuss the case with the daughter. Treatment was discontinued, Mr. Z died peacefully, and no litigation ensued.

Seeking more "facts" to solve ethical or pragmatic problems. This kind of crossed-aspect error demonstrates persistence in thinking about clinical problems as exclusively epistemic-aspect scientific problems. In the context of an ethics conference, a case was presented in which a psychiatrist (Dr. B) had to choose whether or not to inform the fiancée (Ms. X) of the patient (Mr. Y) of his HIV-positive clinical status. To complicate matters, Ms. X was also a patient of Dr. B. The identified problem was the ethics of breaching confidence about Mr. Y's HIV status in order to provide possibly lifesaving information to his fiancée. The questions raised by several residents betrayed discomfort

about grappling with the ethics or values in conflict. They asked questions about the clinical status of Mr. Y and details of the couple's engagement: What signs or symptoms of AIDS or AIDS-related complex did Mr. Y have? How long had Mr. Y been under the physician's care? What was the patient's psychiatric diagnosis? How long had the patient been engaged to Ms. X? Did Mr. Y otherwise have an honest and open relationship with Ms. X? Under what circumstances did Dr. B discover Mr. Y's HIV status?

After this information had been disclosed, the residents came to realize that the new information shed very little light on the problem at hand. A discussion of the conflicting duties, including ethical obligations as well as legal (pragmatic) ones, resulted in a near-consensus on the decision that Dr. B should try first to persuade Mr. Y to tell his fiancée himself, and failing that, Dr. B should inform Ms. X. This example shows that scientifically driven fact gathering can detour decision making that is more efficiently handled within the ethical or pragmatic mode of reasoning. This is not to dismiss the value of scientific inquiry or the acquisition of relevant facts regarding ethical problems. Rather, this example suggests that adding the ethical and pragmatic modes of thinking can be fruitful and efficient. Indeed, crossed-aspect decision making emphasizes the interdependent nature of the three aspects; for example, an inquiry into the values at stake can help in determining the relevant facts, and the relevant facts of the case can shed light on the values at stake.

There are many other possible examples of crossed-aspect failures in clinical decision making. It would be misleading, however, to suggest that a problem in a single face or aspect requires a solution in that aspect—for example, that an ethical problem requires a value-based solution. Frequently, a clinical problem in one aspect can be resolved within another aspect. Reconsider the case of Mr. Y. If Dr. B had been able to persuade Mr. Y to tell his fiancée of his HIV status, Dr. B would have used a pragmatic solution to obviate a more ethically profound decision: to breach or not to breach confidentiality.

DISCUSSION

The biopsychosocial model reflects a particular theory as well as an intended ideal. It is the ideal or spirit that has influenced us the most. The biopsychosocial model, for us, symbolizes humane, empathic, yet rigorous medical care. It is in this spirit that we make the distinction between the importance of the biopsychosocial model and having a concrete method for making humane, empathic, and rigorous clinical decisions.

The clinical method introduced here is intended to render the biopsychosocial model more useful in clinical decision making. As we have argued, however, clinical decision making requires a disciplinary scope much broader than science alone can offer. The three faces or aspects can provide a conceptual shorthand for system-

FIGURE 1. Disciplines Relevant to the Biopsychosocial Model Alone and to the Biopsychosocial Model and the Three Faces Model Considered Together

BIOPSYCHOSOCIAL MODEL	BIOPSYCHOSOCIAL PLUS THREE FACES MODEL
General systems theory	General systems theory
Biology	Biology
Psychology	Psychology
Sociology	Sociology
Anthropology	Anthropology
Other natural/social sciences	Other natural/social sciences
	Health law
	Ethics
	Other philosophy
	Informatics
	Communications theory
	Business management
	Other disciplines

atically examining the breadth of clinical decision making. Figure 1 shows the conceptual scope of the biopsychosocial model and that of the three faces decision-making model described here. It underscores the fact that the complementarity of the three faces model is not simply a matter of semantics. Making biopsychosocial decisions involves ways of reasoning besides scientific thinking. Figure 1 may lead the reader to think that we are adding to the complexity of the biopsychosocial model. In a sense we are, and in a sense we are not. Complexity is suggested by the set of extra formal disciplines that are relevant to biopsychosocial medicine. However, in another way we are not adding complexity. We are not advocating a review of every science in figure 1 before one makes a clinical decision. Indeed, this would counter the demands of the pragmatic face of medicine. With the systems hierarchy, the sciences relevant to psychiatry and medicine are a long list indeed. Should we review each of them before making a clinical decision? With the three aspects described here, clinical problems and decisions can be framed in three interrelated areas without going over each relevant science.

Engel himself recognized the limitation of the biopsychosocial model in problem solving and reconceptualized it in his later work (15) as a model for the science of medicine. To use our language, it is a model for the epistemic aspect of medicine. As such it is an attempt to integrate the pluralism of sciences within medicine. We consider the systems hierarchy essential to research in

psychiatry and medicine, as a theoretical structure for interlevel research problems.

However, the diversity of sciences that embrace the epistemic aspect of medicine may not be the place to look for integration of patient care. It may be through pragmatic and ethical considerations that the wholeness and integrity of the patient can be preserved (34). After all, it is the patient's complaint or need that shapes the inquiries and actions in medicine. Science cannot address patients' needs directly; rather, pragmatic and ethical considerations are required in order to render treatment whole. Patients' practical and moral imperatives direct every therapeutic inquiry and action.

The basic clinical method offered here emphasizes the equivalent importance of epistemic, pragmatic, and ethical considerations in everyday clinical decision making. Further work is needed to describe how the clinician recognizes or distinguishes epistemic, pragmatic, and ethical problems in the clinical encounter. Furthermore, once a problem in a given aspect is recognized, a method is needed for selecting relevant information that contributes to solving the clinical problem (31, 34).

Clinical decision analysis has directed research attention toward clinical decision making and problem solving at least partly to enhance the teaching of clinical skills. However, the majority of work in decision analysis has focused on the problems of diagnosis and treatment (35) (i.e., epistemic aspects), while the incorporation of ethical (36) and practical concerns into these analytic procedures is rare. It seems unlikely that decision analysis will model human clinical decision making accurately without attending to clinical problems *per se* as well as the ethical and pragmatic aspects of medicine.

Research in education has demonstrated the disparity between so-called cognitive knowledge and clinical knowledge (37–40). This disparity is reflected in the three faces of medicine. Cognitive knowledge has to do with what we call the epistemic aspect of medicine, while clinical knowledge would reflect equally the epistemic, ethical, and pragmatic aspects of medicine. Even when we try to define away all but the epistemic aspects of medicine, ethics (36) and pragmatics stubbornly sneak into the problems that confront us. Forrow et al. (41) described the improvement of clinical care that clinical ethics has fostered and the new questions for research that clinical ethics has posed. What new questions does clinical pragmatics pose?

Clinical pragmatics raises questions having to do with taking effective therapeutic action. Some examples could include the following: How do we fund health care for the indigent? What kind of office management facilitates efficient delivery of care? How does a clinician effectively manage the medically ill patient with a personality disorder? What is the best triage system for an emergency room? How do we improve compliance with complicated drug regimens? The disciplines that would deal with these questions would be diverse indeed—biology, psychology, sociology, systems theory, economics, informatics, philosophy, business manage-

ment, and so on. Many of them are not science at all, at least in the formal sense. Many clinicians would claim that these questions have little to do with medicine (42) and certainly not with medical education. Can we afford to not study and teach about the ethical and practical aspects of medicine? Can we practice effective medicine without these considerations?

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Melancholic/Endogenous Depression and Response to Somatic Treatment and Placebo

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Objective: The authors' goals were to examine the effects of somatic treatment and placebo in patients with and without endogenous/melancholic depression. **Method:** Before entry into one of four trials of antidepressant drugs versus placebo, 231 patients were assessed as to whether they met Research Diagnostic Criteria for definite endogenous depression and/or DSM-III criteria for major depressive episode with melancholia. These patients were prospectively assessed for subsequent response to antidepressant treatment or placebo. Previous studies of the effect of endogenous/melancholic depression on treatment response were also reviewed. **Results:** Of the 76 patients with DSM-III melancholia given active medication, 41 (54%) had a complete or partial response, but only 10 (23%) of the 44 patients with melancholia given placebo had a complete or partial response. Of the 76 depressed patients without melancholia given active medication, 46 (61%) had a complete or partial response, and 15 (43%) of the 35 depressed patients without melancholia given placebo had a complete or partial response. Moderately depressed patients with DSM-III melancholia had a significantly better response to active medication than did severely depressed patients with melancholia and showed the greatest difference between response to active medication and response to placebo. The results of the review of previous studies of the effect of endogenous/melancholic depression on treatment response were mixed. **Conclusions:** Depressed patients with melancholia were not particularly different from depressed patients without melancholia in their responses to antidepressant medication but did differ from patients without melancholia in their responses to active medication versus placebo, particularly if their depression was moderate and not severe. This suggests that patients with DSM-III melancholia may be unresponsive to nonsomatic treatments.

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The melancholic and endogenous distinctions for describing depressive illness have been prominent for approximately 60 years (1, 2). It has been presumed that a diagnosis of melancholia or endogenous depression implies a biological rather than an environmental etiology and is usually present in individuals who have little or no maladaptive personality traits. The Research

Diagnostic Criteria (RDC) of Spitzer et al. (3) and APA's DSM-III criteria have assumed a particular pattern of symptoms for endogenous depression or melancholia, respectively, whereby the diagnosis is made according to a fairly similar set of symptom criteria. DSM-III-R includes six symptom criteria for melancholia originally listed in both RDC and DSM-III and also includes three historically based nonsymptom criteria (appendix 1).

Of the three historical criteria, the one that perhaps is most interesting and that we will concern ourselves with here is the inclusion of a "previous good response to specific and adequate somatic therapy." Despite the

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common belief that "melancholics are particularly responsive to somatic treatment" (*DSM-III-R*), there is no research confirming this notion (4). It must be pointed out that many of the studies investigating this question have not examined the prognostic validity of the melancholic and/or endogenous depressive subtypes in relation to a placebo control group.

The main purpose of this paper was to examine prospectively the effects of antidepressants on depressed patients with and without melancholia and/or endogenous depression who participated in one of four antidepressant drug trials. This enabled us to assess whether the presence or absence of melancholic features had a role in response to antidepressant or placebo treatment. We also reviewed the literature examining the effect of endogenous/melancholic depression on treatment response.

METHOD

From June 1984 to June 1988, our group conducted four 6-week antidepressant drug trials: 1) fluoxetine hydrochloride (20–60 mg/day) versus placebo, 2) clovoxamine hydrochloride (100–350 mg/day) versus imipramine hydrochloride (70–245 mg/day) versus placebo, 3) fluoxetine hydrochloride (5–40 mg/day) versus placebo, and 4) paroxetine hydrochloride (10–50 mg/day) versus imipramine hydrochloride (65–275 mg/day) versus placebo. Overall, a total of 313 patients gave voluntary informed consent to participate in one of these four trials. Although there was some variation in the entry criteria for each study, all patients who were involved in these trials had a minimum initial score of 16 on the Hamilton Rating Scale for Depression (5).

At entry into each of these studies, patients were given the Hamilton Rating Scale for Depression (5), the self-rating Beck Depression Inventory (6), the Clinical Global Impression (CGI), the 3-point Raskin Depression Scale (6), and an endogenous depression scale abstracted from the Schedule for Affective Disorders and Schizophrenia—Change Version (7). As a result, we were able to assess whether a depressed outpatient met RDC for *definite* endogenous depression (3). Since the *DSM-III* symptom criteria for major depressive episode with melancholia are all included in the RDC for endogenous depression, we were also able to determine whether a patient met *DSM-III* criteria for melancholia. (As shown in appendix 1, the major difference between the RDC and the *DSM-III* criteria is that anhedonia and lack of reactivity to pleasurable stimuli are required for *DSM-III* melancholia but not for RDC endogenous depression.)

If a patient in any of the four studies met *DSM-III* criteria for major depressive episode and had a minimum score of 16 on the Hamilton Rating Scale for Depression, he or she was placed into a single-blind placebo phase for a mean of 7 days (range=5–10 days). Following the single-blind placebo period, patients were reassessed with the Hamilton Rating Scale for Depression, the Beck Depression Inventory, the CGI, and

TABLE 1. Response to One Week of Placebo Administration of Depressed Patients Who Did or Did Not Meet Criteria for Endogenous/Melancholic Depression

Criteria for Endogenous/Melancholic Depression Met ^a	Responders (N=27) ^b		Nonresponders (N=231)	
	N	%	N	%
Both RDC and <i>DSM-III</i> criteria	5	18.5	100	43.3
Neither RDC nor <i>DSM-III</i> criteria	18	66.7	85	36.8
RDC but not <i>DSM-III</i> criteria	2	7.4	26	11.3
<i>DSM-III</i> criteria but not RDC	2	7.4	20	8.7

^aRDC for endogenous depression, *DSM-III* criteria for major depressive episode with melancholia.

^bThe placebo responders were more likely not to meet both RDC for definite endogenous depression and *DSM-III* criteria for melancholia than were the nonresponders ($\chi^2=9.42$, $df=2$, $p=0.02$).

the Raskin Depression Scale. If a patient's Hamilton score remained above 16 and did not drop more than 20% below the initial value before the single-blind placebo period, the patient was entered into one of the four 6-week double-blind trials of active medication versus placebo. Patients who entered the double-blind phase of these trials were seen and rated weekly with the same scales. At the end of 6 weeks (or 4–5 weeks if that was the endpoint of the study), a determination of response to treatment was made.

Since there is evidence in the literature that fluoxetine (8), clovoxamine (9), and paroxetine (10) have antidepressant efficacy, we combined patients who received these drugs and those who received imipramine into a single antidepressant drug group for the purposes of the data analysis. The placebo group was a combination of the placebo groups from the four individual studies. In addition, we collected data on patients who responded during the 5–10-day single-blind placebo period and compared them with patients who did not respond during this phase.

We decided that a minimum of 4 weeks in the double-blind phase was a sufficient amount of time to determine an adequate response to placebo or active medication. Of the 313 patients who agreed to participate in one of the four studies, 278 entered the double-blind phase. Of the 278, we obtained data on 231 patients, 191 of whom were treated for a full 6 weeks. Using the RDC for *definite* endogenous depression and the *DSM-III* criteria for major depressive episode with melancholia, we examined whether the presence of endogenous/melancholic depression was associated with antidepressant or placebo response.

RESULTS

Table 1 shows the response to 1 week of placebo administration of the patients with and without endogenous and/or melancholic depression who went on to the

TABLE 2. Baseline Depression Scores of Depressed Patients Who Did or Did Not Meet Criteria for Endogenous/Melancholic Depression

Criteria for Endogenous/Melancholic Depression Met ^a	Hamilton Depression Scale Score ^b		Beck Depression Inventory Score ^c		CGI Severity Score ^d		Raskin Scale Score ^e	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Both RDC and <i>DSM-III</i> criteria (N=100)	27.62	5.2	28.83	6.5	4.70	0.8	10.98	1.7
Neither RDC nor <i>DSM-III</i> criteria (N=85)	24.18	5.1	25.79	4.6	4.13	0.6	10.24	1.4
RDC but not <i>DSM-III</i> criteria (N=26)	24.31	4.4	27.11	6.3	4.23	0.7	10.12	1.7
<i>DSM-III</i> criteria but not RDC (N=20)	24.30	4.1	25.60	6.2	4.20	0.6	10.60	1.9

^aRDC for endogenous depression, *DSM-III* criteria for major depressive episode with melancholia.

^bF=8.70, df=3, 227, p<0.0001; Student-Newman-Keuls pairwise comparisons indicated that the group meeting both the RDC and *DSM-III* criteria had significantly higher scores than the other three groups.

^cF=4.79, df=3, 227, p<0.003; Student-Newman-Keuls pairwise comparisons indicated that the group meeting both the RDC and *DSM-III* criteria had significantly higher scores than the group meeting neither set of criteria.

^dF=11.92, df=3, 227, p<0.0001; Student-Newman-Keuls pairwise comparisons indicated that the group meeting both the RDC and *DSM-III* criteria had significantly higher scores than the other three groups.

^eF=4.15, df=3, 227, p<0.007; Student-Newman-Keuls pairwise comparisons indicated that the group meeting both the RDC and *DSM-III* criteria had significantly higher scores than the group meeting neither set of criteria.

TABLE 3. Adjusted Endpoint Mean Scores on the Hamilton Rating Scale for Depression and the Beck Depression Inventory of Depressed Patients Who Did or Did Not Meet Criteria for Endogenous/Melancholic Depression and Were Given Active Medication or Placebo

Criteria for Endogenous/Melancholic Depression Met ^a	Adjusted Mean Score	
	Hamilton Depression Scale	Beck Depression Inventory
Both sets of criteria considered		
Both <i>DSM-III</i> criteria and RDC		
Active medication (N=66)	14.79	14.23
Placebo (N=34)	26.40	26.97
<i>DSM-III</i> criteria but not RDC		
Active medication (N=10)	13.94	13.76
Placebo (N=10)	18.89	19.75
RDC but not <i>DSM-III</i> criteria		
Active medication (N=15)	14.87	16.08
Placebo (N=11)	17.52	19.03
Only <i>DSM-III</i> criteria considered		
Neither <i>DSM-III</i> criteria nor RDC		
Active medication (N=61)	12.88	14.89
Placebo (N=24)	17.85	19.85
<i>DSM-III</i> criteria		
Active medication (N=76)	14.87	14.35
Placebo (N=44)	24.87	25.58
Not <i>DSM-III</i> criteria		
Active medication (N=76)	13.61	15.42
Placebo (N=35)	18.02	19.86

^aRDC for endogenous depression, *DSM-III* criteria for major depressive episode with melancholia.

double-blind phase of the studies. Patients were categorized into four groups according to the presence or absence of RDC endogenous depression and *DSM-III* melancholia. After the 5–10-day single-blind placebo phase, 27 patients exhibited a 50% or greater reduction in their mean Hamilton and Beck scores from the initial screening value. These patients were considered placebo responders. Placebo responders were more likely not to meet both RDC for definite endogenous depression and *DSM-III* criteria for melancholia than were the placebo nonresponders (table 1).

The 231 single-blind placebo nonresponders were given active medication or placebo for at least 4 weeks (191 were treated for a full 6 weeks). Table 2 lists the initial mean Hamilton, Beck, CGI, and Raskin scores of the patients who did or did not meet the criteria for endogenous/melancholic depression. Differences among these groups with respect to initial (baseline) depression scores were examined with two simple one-way analysis of variance (ANOVA) models using scores from the depression scales as the dependent measures. Results of the ANOVA for the Hamilton scale were significant (table 2), and Student-Newman-Keuls post hoc tests revealed that individuals who met both RDC for endogenous depression and *DSM-III* criteria for melancholic depression had significantly higher Hamilton scores than patients in the other three groups. Results of the ANOVA for the Beck scale were also significant (table 2); however, the only significant difference was between patients who had both RDC endogenous depression and *DSM-III* melancholia and those who had neither.

A 4x2 (depression group by treatment group) analysis of covariance (ANCOVA) design with baseline depression score as the covariate was used to examine differences in posttreatment (endpoint) depression score. In considering both RDC and *DSM-III* criteria, in all ANCOVA models, the effect of baseline depression score was significant (p<0.001). For the ANCOVA model on the Hamilton scale, the main effects for depression group (F=3.74, df=3, 222, p=0.012) and for treatment group (F=12.83, df=1, 222, p<0.0001) were significant, but the depression-group-by-treatment-group interaction only approached significance (F=2.26, df=3, 222, p=0.08). For the ANCOVA model on the Beck scale, the main effect for treatment group was significant (F=14.18, df=3, 222, p<0.0001), but the main effect for depression group was not. The depression-group-by-treatment-group interaction was nearly significant (F=2.60, df=3, 222, p=0.053). The adjusted endpoint depression mean scores for the Hamilton and Beck scales are given in table 3.

TABLE 4. Response to Active Medication or Placebo of Depressed Patients With Different Degrees of Depressive Symptoms Who Did or Did Not Meet *DSM-III* Criteria for Major Depressive Episode With Melancholia

Response	Patients Who Met Criteria						Patients Who Did Not Meet Criteria					
	Active Medication			Placebo			Active Medication			Placebo		
	Total	N	%	Total	N	%	Total	N	%	Total	N	%
Patients with moderate depressive symptoms ^a	34			20			61			25		
Complete response		13	38.2		1	5.0		14	23.0		3	12.0
Partial response		12	35.3		5	25.0		23	37.7		9	36.0
No response		9	26.5		14	70.0		24	39.3		13	52.0
Patients with marked to severe depressive symptoms ^b	42			24			15			10		
Complete response		6	14.3		1	4.2		3	20.0		1	10.0
Partial response		10	23.8		5	12.5		6	40.0		2	20.0
No response		26	61.9		20	83.3		6	40.0		7	70.0
All patients ^c	76			44			76			35		
Complete response		19	25.0		2	4.6		17	22.4		4	11.4
Partial response		22	28.9		8	18.2		29	38.2		11	31.4
No response		35	46.1		34	77.3		30	39.5		20	57.1

^aSignificantly higher rates of complete or partial response in the patients who met criteria and were given active medication than in those who met criteria and were given placebo ($\chi^2=11.39$, $df=2$, $p=0.003$) and those who met criteria and were given active medication but started with marked to severe levels of depression ($\chi^2=10.29$, $df=2$, $p=0.006$).

^bNonsignificantly higher rates of complete or partial response in the patients who met criteria and were given active medication than in patients who met criteria and were given placebo ($\chi^2=3.48$, $df=2$, $p=0.18$).

^cSignificantly higher rates of complete or partial response in the patients who met criteria and were given active medication than in those who met criteria and were given placebo ($\chi^2=12.68$, $df=2$, $p=0.002$); nonsignificantly higher rates of complete or partial response in patients who did not meet criteria and were given active medication than in those who did not meet criteria and were given placebo ($\chi^2=3.48$, $df=2$, $p=0.18$).

These data were reanalyzed including only patients who met or did not meet *DSM-III* criteria for melancholia (without consideration of those who met RDC for endogenous depression) for four reasons. First, *DSM-III* criteria are used more universally than the RDC. Second, there was little difference in the absolute baseline and adjusted endpoint depression scores between individuals who had only *DSM-III* melancholia and those who had only RDC endogenous depression. Third, a slightly larger group difference between active medication and placebo was observed for individuals who had only *DSM-III* melancholia than in those who had only RDC endogenous depression. Fourth, collapsing these two groups provided greater statistical power to detect an apparent interaction effect.

The adjusted endpoint mean Hamilton and Beck scores of patients given antidepressant treatment or placebo who did or did not meet *DSM-III* criteria for melancholia are given in table 3. For endpoint Hamilton scores with baseline Hamilton scores as the covariate, the 2×2 (*DSM-III* group by treatment group) ANCOVA found that the *DSM-III* group main effect ($F=8.06$, $df=1$, 226, $p<0.005$), the treatment group main effect ($F=26.82$, $df=1$, 226, $p<0.0001$), and the *DSM-III*-group-by-treatment-group interaction ($F=4.05$, $df=1$, 226, $p=0.045$) were all significant. For endpoint Beck scores with baseline Beck scores as the covariate, the 2×2 (*DSM-III* group by treatment group) ANCOVA found that the treatment group main effect ($F=27.57$, $df=1$, 226, $p<0.0001$) and the *DSM-III*-group-by-treatment-group interaction ($F=4.81$, $df=1$, 226, $p=0.029$) were significant but the *DSM-III* group main effect was not. The formal use of simple main effects for interpretation of

the two significant ANCOVA interactions was not necessary (both factors had only two levels); each revealed that the difference between response to active medication and response to placebo was significant in patients with *DSM-III* melancholia but not in patients without melancholia.

Since individuals who received active medication still had high levels of depression at the endpoint of the study, stringent criteria were used to categorize the patients' response or nonresponse to active medication or placebo. A complete response was defined as having a 50% or greater mean reduction in Hamilton and Beck scores and an absolute endpoint score of 6 or less on the Hamilton scale. A partial response was defined as having just a 50% or greater mean reduction in Hamilton and Beck scores. Failure to meet either set of criteria was defined as nonresponse. Using these categories and the presence or absence of *DSM-III* melancholia, we performed a chi-square analysis on the relative rates of response to active medication and placebo. The results indicated that the 76 patients with *DSM-III* melancholia given active medication had a significantly higher rate of complete or partial response than did the 44 patients with *DSM-III* melancholia given placebo but that the 76 patients without *DSM-III* melancholia given active medication did not have a significantly different rate of complete or partial response than did the 35 patients without *DSM-III* melancholia given placebo (table 4).

The patients given the drugs approved by the Food and Drug Administration (FDA) (imipramine and fluoxetine) showed the same differential response to active medication and placebo when considered individu-

ally. That is, patients with *DSM-III* melancholia who were given imipramine had a complete or partial response rate of 60.9%, but patients with melancholia who were given placebo had a complete or partial response rate of only 22.7% ($\chi^2=7.57$, $df=1$, $p=0.005$); patients without melancholia who were given imipramine had a complete or partial response rate of 73.7%, and patients without melancholia who were given placebo had a complete or partial response rate of 44.9% ($\chi^2=3.34$, $df=1$, $p=0.09$). For fluoxetine, the active medication and placebo response rates for patients with melancholia were 55.6% and 22.7% ($\chi^2=7.76$, $df=1$, $p=0.006$), respectively, but the active medication and placebo response rates for patients without melancholia were 53.3% and 44.9% ($\chi^2=0.44$, $df=1$, $p=0.50$), respectively. The drugs not approved by the FDA (clovoxamine and paroxetine) showed an overall difference between drug and placebo. This is, depressed patients with and without melancholia who were given these drugs or placebo had statistically different response rates to active medication and placebo (54.5% versus 31.6%) ($\chi^2=6.75$, $df=2$, $p<0.04$). However, when the patients were divided into those with and those without melancholia, the number of subjects in each group was too small to obtain statistically significant results.

We subdivided all of the patients with and without *DSM-III* melancholia by whether they started with moderate (CGI score of 4) or marked to severe (CGI score of 5 or 6) levels of depression and examined the response rates to active medication and placebo. The results of this analysis are given in table 4. The best response to active medication was shown by the patients with melancholia who started with moderate depression: 74% of these patients had a complete or partial response to active medication, compared with 38% of the patients with melancholia given active medication who started with marked to severe depression and 30% of the patients with melancholia given placebo who started with moderate depression. The response rate to active medication of the patients with melancholia who started with marked to severe depression was not significantly higher than the response rate to placebo of patients with melancholia who started with marked to severe depression.

It should be noted that the differential between response to active medication and response to placebo for the moderately and severely depressed groups was similar for patients who underwent 6 weeks of treatment ($N=191$) and those who were treated for only 4–5 weeks ($N=40$). Of the 37 severely depressed patients with melancholia who underwent a full 6 weeks of treatment with active medication, 16 (43.2%) had a complete or partial response; of the 16 severely depressed patients with melancholia who underwent a full 6 weeks of treatment with placebo, four (25%) had a complete or partial response ($\chi^2=0.90$, $df=1$, $p=0.34$), which argues against the idea that nonresponse in this group of severely depressed patients was due merely to an insufficient amount of time for drug efficacy (11, 12).

DISCUSSION

Previous studies examining the effect of endogenous/melancholic depression on treatment response (13–38), summarized in tables 5–8, have had mixed results. It must be pointed out that only a few of the studies were specifically designed to assess the prognostic validity of melancholic/endogenous subtyping. The majority of these studies either assessed a variety of factors regarding the prognostic validity of drug response (one of which was the presence or absence of endogenous depression) or were placebo-controlled studies assessing whether a particular treatment was efficacious and merely noted the presence or absence of endogenous/melancholic features for each patient in the trial.

The majority of the studies that examined somatic treatments in patients with or without endogenous/melancholic depression with no placebo control group (13–18) or without comment on a placebo control group (19–23) suggested that the presence of endogenous/melancholic depression did not predict a good response to somatic treatment (table 5). If there had been no placebo control groups for the four studies reported here, we would have made the same conclusion, because the results showed that there was no difference between the *DSM-III* groups with respect to drug response. It is interesting to note that Davidson et al. (21–23) found that when RDC for endogenous depression were applied, 70% of the patients with nonendogenous depression, compared with 45% of the patients with endogenous depression, responded to isocarboxazid according to scores on the Hamilton scale. When *DSM-III* criteria for melancholia were applied, they found that 65% of the patients without melancholia responded to isocarboxazid compared with 43% of those with melancholia.

Although the presence of endogenous/melancholic symptoms is thought to predict a poor response to nonbiological therapies, the three studies on this topic (24–26) were inconclusive (table 6). Prusoff et al. (24) found that patients with endogenous symptoms had a poor response to interpersonal psychotherapy, unlike patients without endogenous symptoms. Two other studies of cognitive therapy compared with pharmacotherapy (25, 26), however, found that the presence or absence of endogenous depression did not predict response to cognitive therapy, pharmacotherapy, or a combination of these two treatments.

Studies that evaluated patients with and without endogenous/melancholic depression given either placebo (27, 28) or no treatment (29) have yielded mixed results (table 7). Rabkin et al. (27) found that 36% of the patients who initially responded to placebo and subsequently relapsed had a diagnosis of endogenous depression, compared with 24% of those who remained well. Fairchild et al. (28) found that only one of 21 patients who responded to placebo after 1 or 5 weeks had RDC-diagnosed endogenous depression but that 17 of 34 patients who did not respond to placebo had endogenous depression. This study had a flaw in that

TABLE 5. Studies That Evaluated Medication and/or Somatic Treatments Without Placebo Group or Without Comment on a Placebo Group in Depressed Patients With or Without Endogenous/Melancholic Depression

Study	Year	Design	Patients	Results and Comments
Coryell et al. (13)	1980	Evaluated predictors of response in depressed outpatients treated with amitriptyline or nortriptyline treated for 6 weeks	44 patients	Presence or absence of specific endogenous or nonendogenous symptoms did not predict response to either drug
Kupfer and Spiker (14)	1981	Evaluated clinical predictors in inpatients treated with amitriptyline for at least 2 weeks	Of 76 patients, 54 had endogenous symptoms	Presence of endogenous depression did not predict good response
Razani et al. (15)	1983	Evaluated efficacy of amitriptyline, tranylcypromine, and amitriptyline plus tranylcypromine in treating major depression	Of 60 patients randomized to three groups, 22 met <i>DSM-III</i> criteria for melancholia	Presence or absence of melancholia did not predict response to any treatment
Coryell and Zimmerman (16)	1984	Evaluated predictors of response in patients with major depression treated with ECT	31 patients with major depression treated with at least six ECTs	Presence or absence of <i>DSM-III</i> melancholia did not predict response to ECT
Coryell and Turner (17)	1985	Evaluated efficacy of desipramine in patients with major depression over 6 weeks after a 1-week single-blind placebo period	Of 42 patients, seven had 30% decrease in depression scores; 35 patients received desipramine for at least 2 weeks	Presence or absence of endogenous diagnosis did not predict response to desipramine
Sauer et al. (18)	1986	Patients with major depression treated with amitriptyline for 3 weeks	Of 50 patients, 26 (52%) met <i>DSM-III</i> criteria for melancholia, 24 (48%) had endogenous symptoms according to Newcastle scale (score of 6 or higher)	No correlation between drug response and <i>DSM-III</i> melancholia or between drug response and absolute Newcastle score; trend for more improvement in patients with moderate Newcastle scores than in patients with low or high Newcastle scores
Georgotas et al. (19)	1987	Evaluated <i>DSM-III</i> melancholia and RDC and Newcastle endogenous depression; patients 55 and older treated with nortriptyline, phenelzine, or placebo for 6-7 weeks	Of 42 patients, 23 given nortriptyline and 19 given phenelzine	Presence or absence of RDC endogenous depression, <i>DSM-III</i> melancholia, or Newcastle endogenous depression did not significantly affect response rate
Paykel et al. (20)	1988	General practice patients with depression treated with amitriptyline or placebo over 6 weeks	141 patients treated for at least 4 weeks; about 30% had endogenous symptoms	No correlation between presence and absence of RDC endogenous symptoms, between sex and Present State Examination scores, or between endogenous-neurotic index and drug response
Davidson et al. (21-23)	1983, 1984	Evaluated efficacy of isocarboxazid versus placebo or two doses of isocarboxazid over 4 weeks in patients with depression	50 patients received isocarboxazid; 14 received placebo	Patients without endogenous/melancholic depression had a better response to isocarboxazid than those with endogenous/melancholic depression

it was questionable whether there are differences between patients who respond to placebo after 1 week and those who respond after 5 weeks. Nelson et al. (29) found that only one of 18 patients with *DSM-III* melancholia responded to the nonspecific effects of hospitalization but that 18 of 37 depressed patients without melancholia responded to hospitalization. They also found that 23 of 30 patients with melancholia compared with 12 of 20 patients without melancholia responded to desipramine.

Studies evaluating patients with and without endogenous/melancholic depression with respect to response to active medication versus placebo (30-38) have also yielded mixed results (table 8). Raskin and Crook (30) found that patients with endogenous depression re-

sponded favorably to chlorpromazine and imipramine but not to placebo. The criteria for endogenous depression in this study were not based on current classification systems. In a subsequent study, Paykel et al. (31) found that depressed patients with and without endogenous depression who were given either amitriptyline or phenelzine showed a statistically significant difference in responses to active medication versus placebo. Stewart et al. (32, 33) reported that among patients with RDC endogenous depression, 11 of 16 responded to desipramine and six of 17 responded to placebo; among patients with *DSM-III* melancholia, two of four responded to desipramine and none of seven responded to placebo. There was a trend toward a difference in response to active medication versus placebo among

TABLE 6. Studies That Evaluated Medication and Nonbiological Treatments Without Placebo Group in Depressed Patients With or Without Endogenous/Melancholic Depression

Study	Year	Design	Patients	Results and Comments
Prusoff et al. (24)	1980	Patients with major depression treated with pharmacotherapy (amitriptyline), interpersonal psychotherapy, combination of pharmacotherapy and psychotherapy, or nonscheduled control treatment	Of 81 patients, 26 had definite endogenous symptoms and 55 had either probable endogenous or no endogenous symptoms	Patients with endogenous symptoms had worse response to interpersonal therapy alone than did patients without endogenous symptoms; no difference between patients with and without endogenous symptoms for other three treatment conditions
Blackburn et al. (25)	1981	12-week trial assessed cognitive therapy, pharmacotherapy (amitriptyline or clomipramine), or combination of pharmacotherapy and cognitive therapy	Of 64 patients, 22 received cognitive therapy, 20 received pharmacotherapy, and 22 received combination	No difference between initial endogenous status and response to three treatments
Kovacs et al. (26)	1981	12-week trial assessed cognitive therapy versus pharmacotherapy (imipramine) in outpatients with depression	Of 44 patients, 19 received cognitive therapy and 25 received pharmacotherapy	Degree of endogenous features did not predict response to pharmacotherapy or cognitive therapy

TABLE 7. Studies That Primarily Evaluated Response to Placebo in Depressed Patients With or Without Endogenous/Melancholic Depression

Study	Year	Design	Patients	Results and Comments
Rabkin et al. (27)	1986	Evaluated patients with depression who had responded to single-blind placebo 3 months earlier	Of 45 patients, 20 remained well and 25 relapsed	Diagnosis of endogenous depression did not predict subsequent relapse
Fairchild et al. (28)	1986	Evaluated characteristics of 1-week single-blind and 5-week double-blind placebo response	16 patients who responded to 1-week placebo; five who responded to 5-week placebo; 34 who did not respond to placebo	More of the placebo nonresponders had an RDC diagnosis of endogenous depression
Nelson et al. (29)	1990	Evaluated patients with major depression after 1 week of hospitalization; patients who did not respond to hospitalization were treated with desipramine for 4 weeks	87 patients initially evaluated; <i>DSM-III</i> melancholia status was defined in 56; 52 patients required treatment with desipramine	More patients without melancholia responded to hospitalization; slightly more patients with melancholia responded to desipramine

patients with endogenous/melancholic depression, but the number of patients was too small to draw any conclusions. Rickels et al. (34) found that patients with endogenous depression displayed a trend toward different responses to active medication and placebo but that depressed patients without endogenous depression did not. (The diagnosis of endogenous depression was made by clinical judgment.) When Rickels et al. used *DSM-III* criteria for melancholia, they found that patients with and without melancholia did not differ in their response to active medication versus placebo. Zisook et al. (35) studied patients who had atypical depression and found that the presence of endogenous depression did not predict differential responses between active medication and placebo. Rabkin et al. (36) found that 41% of 1-week placebo responders, 52% of 6-week placebo responders, 49% of 6-week placebo nonresponders, 50% of 6-week active medication responders, and 42% of 6-week active medication nonresponders had endogenous depression. Fairchild and Rush (37) reported that 13 of 14 patients with endogenous depression responded to amitriptyline and that

four of nine patients with endogenous depression responded to placebo. Finally, Reimherr et al. (38) noted that in a group of patients with *DSM-III* melancholia, 64% responded to sertraline, 68% responded to amitriptyline, and 38% responded to placebo. In a group of patients without *DSM-III* melancholia, 58% responded to sertraline, 65% responded to amitriptyline, and 44% responded to placebo. Response was determined by a final CGI score of 1 or 2.

The results of our current study suggest that the presence of melancholic symptoms is associated with differential responses to active medication and placebo and generally predicts a poorer response to placebo. Therefore, there may be a greater need for antidepressant medication in the treatment of melancholic symptoms than nonmelancholic symptoms. Melancholic symptoms are not necessarily more predictive of a favorable response to somatic treatment, as evidenced by similar rates of complete or partial response to active medication for patients with melancholia (54%) and those without (61%).

One important reason for the lack of differentiation

TABLE 8. Studies That Evaluated Response to Active Medication and Placebo in Depressed Patients With or Without Endogenous/Melancholic Depression

Study	Year	Design	Patients	Results and Comments
Raskin and Crook (30)	1976	Retrospectively evaluated 880 patients treated in clinical trials with placebo, imipramine, or chlorpromazine	135 patients classified as endogenous	Endogenous patients responded well to imipramine and chlorpromazine but not to placebo; patients without endogenous symptoms showed no difference in response to three treatments
Paykel et al. (31)	1982	Evaluated response of depressed patients treated for 6 weeks	131 depressed patients treated with amitriptyline, phenelzine, or placebo	No significant differences in response to amitriptyline or phenelzine between patients with and without endogenous symptoms; both drugs were statistically superior to placebo for both groups
Stewart et al. (32, 33)	1983, 1985	Evaluated treatment response characteristics of patients with RDC endogenous depression (32) or <i>DSM-III</i> melancholia (33)	103 patients treated with either desipramine or placebo; same treatment group for both evaluations	More patients with endogenous depression and melancholia responded to desipramine than to placebo, but number of patients was too small to define statistical significance
Rickels et al. (34)	1985	Evaluated alprazolam versus doxepin, amitriptyline, and placebo in treating depression; then evaluated whether patients met <i>DSM-III</i> criteria for melancholia	504 outpatients with major depression began treatment; 348 classified endogenous and 143 classified nonendogenous; 154 had <i>DSM-III</i> melancholia and 338 did not	Group with endogenous depression seemed to show a difference between drug and placebo response; group without endogenous depression did not; <i>DSM-III</i> melancholia did not predict a greater difference between drug and placebo response
Zisook et al. (35)	1985	Evaluated isocarboxazid versus placebo in treating atypical depression	69 patients randomized to isocarboxazid or placebo; 24 (35%) had RDC endogenous depression	Presence of endogenous depression did not predict differential response to isocarboxazid versus placebo
Rabkin et al. (36)	1987	Evaluated effect of numerous factors on treatment response in patients with depressive illness	Pooled data on 484 patients from several studies; 143 1-week (N=94) and 6-week (N=49) placebo responders, 117 6-week placebo nonresponders, and 224 6-week drug responders (N=135) and 6-week drug nonresponders (N=89)	Presence or absence of endogenous diagnosis did not produce significantly different response rates in the five placebo or active medication groups
Fairchild and Rush (37)	1989	Patients with endogenous depression randomized to amitriptyline or placebo	Of 23 patients, 14 given amitriptyline and 9 given placebo	Most patients given amitriptyline responded; almost half of the patients given placebo responded
Reimherr et al. (38)	1990	Patients with major depression treated with sertraline, amitriptyline, or placebo for 6 weeks	Of 448 patients, 168 met <i>DSM-III</i> criteria for melancholia	Patients with melancholia had greater difference in active drug response versus placebo response than patients without melancholia. Both groups had statistically significant differences in active drug response versus placebo response

in response to drug versus response to placebo between melancholic and nonmelancholic patients in previous studies may be the severity of illness. Studies examining RDC endogenous depression and *DSM-III* melancholia noted that patients with endogenous/melancholic depression have more intense depression (21, 39, 40). Indeed, in our study, patients who met criteria for both

endogenous depression and melancholia had higher baseline Hamilton, Beck, CGI, and Raskin scores than patients who met neither (table 2). However, when we subdivided our patients into those with moderate or marked to severe depression, we found that patients who had *DSM-III* melancholia and moderate depression had the best response rates. These results are in line

with the work of Sauer et al. (18), Abou-Saleh and Coppen (41), Rao and Coppen (42), and Milln and Coppen (43). Abou-Saleh and Coppen (41) found that patients whose Newcastle endogenous depression scores were in the middle range responded significantly better than patients scoring in the upper range, who had more intense depression as indicated by higher Hamilton scores.

Our finding that moderately depressed patients responded better than severely depressed patients (particularly among patients with melancholia) is consistent with the work of Kocsis et al. (44), who found that moderately depressed patients had a 67% response rate and severely depressed patients had a 39% response rate in a sample of 132 subjects who were treated for 4 weeks with either amitriptyline or imipramine.

As noted in table 4, depressed patients without *DSM-III* melancholia did not show a difference between active medication and placebo (likely due to the small number of patients in each group), but there was a nonsignificantly higher rate of response to active medication than to placebo in the severely depressed group. This should not be taken to mean that drugs are ineffective for this patient group. There is evidence for a favorable response to antidepressants in the treatment of nonendogenous depression (45). Indeed, studies on patients with atypical depression who had primarily but not exclusively nonendogenous depression (32, 46, 47) have shown that there are notable differences between responses to active medication and placebo in such patient groups. These studies have also revealed that patients with nonendogenous depression plus anxiety, panic, or hysteroid dysphoria may preferentially respond to monoamine oxidase inhibitors over tricyclics (48–50), although this has not been confirmed by all studies (31, 51, 52). This evidence clearly supports the utility of drug therapy for nonendogenous depression, which generally is less severe than endogenous depression. However, other studies have shown that when the severity of depression falls below a minimal level (i.e., Hamilton score of 13–14), there may be no detectable difference between active medication and placebo (20, 32).

The findings of this study are not at odds with those in the literature reviewed here. As noted in table 4, depressed patients without melancholia had a nonsignificantly higher rate of complete or partial response to active medication than to placebo. Clearly, depressed patients with and without melancholia showed a response to antidepressant treatment, but the patients with melancholia displayed a much larger difference between their response to active medication and their response to placebo.

CONCLUSIONS

This study does not support the idea propounded in *DSM-III-R* that depressed individuals with melancholia are particularly responsive to somatic treatment. We found that depressed patients with *DSM-III* melanco-

lia did not respond to antidepressant treatment any better than did patients without *DSM-III* melancholia. Rather, it appeared that the patients with *DSM-III* melancholia showed a greater difference between their response to active medication and their response to placebo than the depressed patients without melancholia, particularly when the level of initial depression was of moderate rather than severe intensity. This finding suggests that patients who have *DSM-III* melancholia may be unresponsive to nonsomatic treatments. Future double-blind placebo-controlled trials are needed to assess the predictive validity of the endogenous/melancholic subtype.

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APPENDIX 1. DSM-III and DSM-III-R Criteria for Major Depressive Episode With Melancholia and RDC for Endogenous Depression

DSM-III CRITERIA

The presence of at least five of the following:

1. Loss of pleasure in all or almost all activities
2. Lack of reactivity to usually pleasurable stimuli
3. At least three of the following:
 - a. Distinct quality of depressed mood
 - b. Depression usually worse in morning
 - c. Early morning awakening (at least 2 hours before the usual time)
 - d. Marked psychomotor retardation or agitation
 - e. Significant anorexia or weight loss
 - f. Excessive or inappropriate guilt

DSM-III-R CRITERIA

The presence of at least five of the following:

1. Loss of pleasure in all or almost all activities
2. Lack of reactivity to usually pleasurable stimuli
3. Depression regularly worse in morning
4. Early morning awakening (at least 2 hours before the usual time)
5. Marked psychomotor retardation or agitation (not merely subjective complaints)
6. Significant anorexia or weight loss (more than 5% body weight in a month)
7. No significant personality disturbance before first major depressive episode
8. One or more previous major depressive episodes followed by complete or nearly complete recovery

9. Previous good response to specific and adequate somatic antidepressant treatment

RDC

From groups A and B, a total of four symptoms for probable and six for definite, including one symptom from A:

Group A

1. Distinct quality of depressed mood
2. Lack of reactivity to usually pleasurable stimuli

3. Depression usually worse in morning
4. Loss of pleasure in all or almost all activities

Group B

1. Excessive or inappropriate guilt
2. Early morning awakening or middle insomnia
3. Psychomotor retardation or agitation
4. Poor appetite
5. Weight loss
6. Loss of interest or pleasure in usual activity or decreased sex drive

Initial Findings on Preventive Intervention for Families With Parental Affective Disorders

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Objective: The purpose of this study was to develop a clinician-based cognitive, psychoeducational, preventive intervention for families with parental affective disorder that would be suitable to widespread use, test its feasibility and safety, and define the areas affected by the intervention. The intervention was designed to increase understanding of parental illness and resilience in the children. **Method:** The authors studied the first seven families (14 parents) to receive the intervention. Enrollment criteria included affective disorder during the preceding year in at least one parent, presence of at least one child between the ages of 8 and 14 years who was not psychiatrically ill at the time of participation, and willingness to participate in the research study. The intervention consisted of parent, child, and family sessions. Assessment included semistructured interviews with parents about affective disorders, standard ratings of marital satisfaction and therapeutic alliance, and a recently developed semistructured interview to assess response to the intervention. **Results:** Overall satisfaction with the intervention was rated moderate to high by parents. No harm was reported. Ten of 14 parent subjects reported five or more behavior and attitude changes that they attributed to the intervention. The most frequent behavior and attitudinal changes reported were increased discussion of the illness and related issues and increased understanding of information about affective illness. **Conclusions:** The authors conclude that the intervention is safe and feasible in families with parental affective disorder.

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A consensus from a variety of perspectives (1-4) supports the need for preventive intervention strategies for children of parents with affective disorders (5). As recent reviews have documented (6-9), there is compelling evidence that the children of parents with affective disorder fare more poorly than comparison samples whose parents have not experienced affective disorder. In particular, the children have high rates of depression as well as other areas of impairment.

Specific criteria have been identified for empirical research in prevention that have guided the design and implementation of this study (10, 11). These are 1) that the research involve clearly defined populations at risk, 2) that the risk be well-established, 3) that the interven-

tion be targeted to specific dimensions, 4) that it be expected to have a long-term effect, and 5) that evaluation be rigorous and use standard instruments (10, 11). In the development of new preventive strategies, Offord (11) has argued persuasively that it is essential to establish that the intervention does more good than harm. That was especially important in this project, since the intervention involved families not seeking treatment for their children. Thus, the possibility that it might be disruptive or harmful had to be considered seriously.

The aims of this investigation were to develop a clinician-based psychoeducational intervention that would be suitable for widespread use, test its feasibility and safety, and define the areas affected by the intervention. We have chosen to report on the first seven families receiving the intervention because the number is large enough to explore the safety and feasibility of the approach.

THE PREVENTIVE INTERVENTION APPROACH—SHORT-TERM, COGNITIVE, AND PSYCHOEDUCATIONAL

The intervention consists of six to 10 sessions and includes individual sessions with parents and children

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and one or two family meetings. The clinician is available to the family throughout the time of the intervention and thereafter by telephone. The core elements of the intervention are 1) assessment of all family members, 2) teaching of information about affective disorders and risks and resilience in children, 3) linking of this information to the individual's and family's life experience, and 4) enhancement of the child's understanding of the illness and development of concrete plans for helping the child cope in the future. The intervention has a strong cognitive orientation because cognitive approaches to treatment have proved successful in addressing the distortions of depression. Beardslee and Podorefsky's study (12) of the role of self-understanding in children growing up in homes with serious affective disorder also guided the design of the intervention. It emphasized the importance of self-understanding, in particular, being separate from their parents and able to take independent actions as essential dimensions of these children's ability to cope with and master the difficulties in living with a severely depressed parent. Eisenberg's observation (13) of the distinction between the diagnosis of disorder and the individual family's experience of illness provided an important conceptual frame. Our focus is on the illness experience. Given the heterogeneity of affective disorders in parents, it has proved essential to understand the child's and the family's specific experience of illness. Finally, our approach was designed for use by a wide range of practitioners who treat adults with affective disorder, especially general psychiatrists, internists, family practitioners, and pediatricians. The intervention has been described elsewhere (14), and a manual has been developed for training clinicians and for its implementation (available on request from the first author).

While there is evidence that children are at risk at every age, a target population of children ages 8–14 years was selected for this study because of the dramatic increase in the prevalence of affective disorders during adolescence. In addition, children in this age range begin to function autonomously and have the ability to understand causation in relation to the parental disorder.

METHOD

Design

Families were recruited from a prepaid health plan, local psychiatric hospitals, and general medical hospitals. The intervention was described as a research project that offered preventive intervention services and compared two forms of intervention. It was free and voluntary. Appropriate human studies permissions were obtained. Enrollment criteria for parents included a history of serious parental affective disorder in the recent past; at least one child, aged 8–14, not currently seriously disturbed; the absence of schizophrenia, organic brain damage, and current drug or alcohol addiction in the parents (although other psychiatric disorders

could coexist); the absence of a current life crisis; and the presence of a professional who was treating the adult affective disorder or could be involved should such treatment be necessary. Two-parent families are the subject of the current report, although the intervention has been used successfully with single-parent families. Families were randomly assigned on a two-thirds/one-third basis to a clinician-based psychoeducational, preventive intervention or to a lecture comparison group. A larger number of families were included in the clinician-based intervention because the evaluation of the safety of this intervention was a central aim of the initial study.

Implementation of the Intervention

Clinicians underwent an extensive training program to ensure that the intervention was delivered in a standard fashion. The training included a detailed review of transcribed cases, frequent meetings for supervision, and use of actors in a simulation of the intervention with videotaping for later review. In addition, ongoing supervision was provided.

Measures

Measures were administered separately to each parent by trained raters who were blind to any information about the intervention.

Adult psychopathology. The Schedule for Affective Disorders and Schizophrenia—Lifetime Version (SADS-L) (15) was employed to measure psychopathology in the parents before the intervention. It is a widely used interview that makes diagnoses according to Research Diagnostic Criteria (16). The validity of the SADS-L has been established in a wide range of studies.

Marital adjustment. The Dyadic Adjustment Scale (17), a self-report, was used to measure marital satisfaction and was completed by each parent before and after the intervention. The overall scale has demonstrated internal consistency and external validity (17).

Therapeutic alliance. We examined the therapeutic alliance in the family context using the Integrative Psychotherapy Alliance Scales (18). From the Integrative Psychotherapy Alliance Scales, two self-report scales were completed by each parent, assessing the individual's relationship with the therapist and the couple's relationship with the therapist as viewed by the respondent.

Semistructured interview about the intervention. A review of existing assessment literature revealed that several of the main dimensions targeted by our intervention, i.e., specific behaviors and attitudes that we hoped to change or modify, were not covered by existing quantitative instruments. We developed an interview designed to elicit both qualitative information about the experience of families and quantitative ratings by using 7-point Likert-type scales (19). Subsections assess the parent's prior factual knowledge of affective illness including risk factors for children and characteristics of resilient children, the parent's experi-

ence of illness in the family, the effect of the illness on the couple's relationship, the effect of the illness on the children, and concerns related to the illness. The postintervention assessment contains additional questions and self-rating scales about the parent's experience with the intervention and its helpfulness. The following four categories of ratings obtained from the semistructured interview about the intervention will be reported in this paper.

1. During the postintervention assessment, parents were asked to rate overall satisfaction with the intervention, the degree of helpfulness of the intervention in several areas (e.g., communication between parent and child concerning the illness, supportiveness of the spouse), and dissatisfaction or possible harmful effects.

2. During the pre- and postintervention interviews, parents were asked to identify up to three separate illness-related concerns. These concerns were then rated by the parent for degree of upset before and after the intervention; degree of helpfulness provided by the intervention was also rated. The ratings of concerns were modeled after the target problems approach (20) that has been used in psychotherapy research and that enables patients to identify and rate the unique problems they want to address in psychotherapy.

3. Scores of reported behavior and attitude changes that parents attributed at least in part to the intervention were obtained by examining the content of the pre- and postintervention interviews. The scoring system was developed for this study. Interrater reliability was established.

4. Self-ratings of functioning in the couples' and family relationships during the month before the interview were obtained before and after the intervention (e.g., degree to which couple's communication is disrupted by the affective illness, degree to which the affective illness has an impact on child-related tasks).

Subjects

The first seven families who completed the intervention form the cohort. The identified patients in the couples suffered significant affective disorder measured on the SADS-L (15), as indicated by the average lifetime duration of all forms of affective disorder, which was 10.2 years ($SD=15.3$). The shortest lifetime duration reported was 10 months. The lifetime diagnoses of these seven patients included bipolar I disorder ($N=2$; one also met criteria for schizoaffective disorder), major depressive disorder ($N=2$), and bipolar II disorder ($N=3$). In addition, the patients had associated nonaffective diagnoses. Moreover, within the past year, four identified patients were diagnosed with unipolar depressive disorders (one of these also had a diagnosed episode of schizoaffective disorder), two had bipolar II disorder (with an episode of depression), and one patient had bipolar II disorder but denied an episode in the past year, although the patient was still taking medication. There was a high rate of dual-parent lifetime illness. Both spouses in four couples (57%) had SADS-L diag-

noses (including anxiety and substance abuse disorders) at some point in their lifetime. All seven families fell within the top two socioeconomic levels on the Hollingshead-Redlich classification (21). The Dyadic Adjustment Scale provides an overall rating of marital adjustment that can be compared to available group norms. Our cohort of seven couples had a mean Dyadic Adjustment Scale score of 108.1 ($SD=12.7$), which falls below the scale's mean for married couples (mean=114.8, $SD=17.8$) but is substantially above the mean for divorced couples (mean=70.7, $SD=23.8$) (17). The mean age of children in the study was 10.9 years ($SD=2.0$) ($N=8$). Families had an average of one child in the age range.

RESULTS

Satisfaction and Safety

Average overall satisfaction (mean=5.29, $SD=1.73$) fell between moderately (scale value=4) and extremely (scale value=7) satisfied. Scores ranged from 1 (not at all satisfied) (1 parent) to 7 (extremely satisfied) (three parents). Mean satisfaction with the presentation of factual information during the intervention also was above the moderate level (mean=5.36, $SD=1.39$). Ratings varied from 3 ($N=2$) to 7 ($N=3$). Average scores for the more specific satisfaction ratings showed more variability, although most did not fall below the moderate level.

Ratings of therapeutic alliance provided an additional indication of overall satisfaction with the intervention. The mean individual alliance score for the 14 participants was 5.4 ($SD=0.8$) (possible range=1-7), and the mean couples alliance score was 5.5 ($SD=0.7$). Parents generally agreed with positive statements about the relationship of the therapist to the respondent (parent) and to the couple. No parent reported a negative therapeutic alliance, as indicated by a score of 3 or below.

Three postintervention 7-point Likert scales gave the parents the opportunity to rate the intervention directly for degree of dissatisfaction or harmfulness (1=not at all, 7=a great deal). Overall, parents reported no harm from the intervention. Means, standard deviations, and ranges were as follows: 1) Did the intervention make it more difficult to talk to your spouse about your illness: mean=1.21, $SD=0.4$, range=1 ($N=11$) to 2 ($N=3$); 2) Did the intervention make communication between you and your children worse: mean=1.0, $SD=0.0$; 3) Is your relationship with your children worse now that you have participated in the intervention: mean=1.36, $SD=1.34$, range=1 ($N=13$) to 6 ($N=1$). One parent in the same section gave a rating of 6 for making her relationship better with her children and a rating of 6 for making her relationship with her children worse. We believe that this was the parent's misunderstanding of the question because all of her other ratings of the intervention, including overall satisfaction, were positive, as were her husband's.

TABLE 1. Reported Changes in Behavior and Attitude/Cognitive Understanding in 14 Parents Who Received Preventive Intervention for Families With Parental Affective Illness

Area and Number of Changes Reported	N	%
Behavior		
0	2	14.3
1	3	21.4
2	3	21.4
3 or more	6	42.9
Attitude/cognitive understanding		
0	0	0.0
1	2	14.3
2	2	14.3
3	1	7.1
4 or more	9	64.3
Combined attitude and behavior		
0	0	0.0
1	1	7.1
2	1	7.1
3	2	14.3
4 or more	10	71.4

Self-ratings of couples and family functioning on the Dyadic Adjustment Scale and the semistructured interview about the intervention did not show significant change at postassessment.

Individual Concerns

On average, parents' degree of upset for the first and second illness-related concerns fell at the above moderate level (concern 1: mean=5.57, SD=1.40; concern 2: mean=4.50, SD=1.91). Mean postintervention degree of upset was 4.43 (SD=1.65) for the first concern and 3.86 (SD=1.35) for the second concern. Parents reported significantly less upset for the primary concern after the intervention (Wilcoxon matched-pairs signed ranks test: $T=23$, $p=0.04$). They also reported moderate help from the intervention for each of the concerns (concern 1: mean=3.86, SD=1.99; concern 2: mean=4.29, SD=2.13). All seven families cited concerns about their children as one of their three most pressing concerns. They were about evenly divided between worries about the future and immediate concerns about their children's responses to the affective illness.

Behavior and Attitude Changes

Eighty-six percent ($N=12$) of the parents reported at least one change in behavior that could be attributed to participation in the intervention, and 100% reported at least one change in attitude or belief about illness-related issues (table 1). Ten of the 14 parents reported at least four or more combined behavior and attitude changes. The most frequent behavior change reported by parents was increased discussion of the illness and related issues within the couple, among other family members, with children, and/or with persons outside the home. Attitudinal and cognitive changes most frequently reported were increased understanding of in-

formation about affective illness as it relates to the adult and risk and resilience factors in children. Some parents also reported that they believed their children better understood their illness. Several parents reported a sense of reassurance and destigmatization of the illness.

CASE REPORT

The family consisted of the mother, father, and three children: a 14-year-old girl who had been in residential care for the past 3 years, a 9-year-old boy, and a 2-year-old girl. The intervention took place in seven sessions, one with the family, one with the boy alone, and five with the couple. The mother, the identified patient, had suffered with depression since college. Throughout adulthood she had had recurrent episodes of dysthymia exacerbated by the stress of caring for her severely handicapped 14-year-old daughter. The mother's first psychiatric hospitalization occurred when her elder daughter became critically ill for a second time. Her son was then 4. Six months before the intervention, the mother had again become depressed. She had been placed on a regimen of medication and was being followed by a psychotherapist.

During the first two sessions, information on the couple's experience with the illness was obtained, first from the mother, then from the father, and finally from both parents' view of the child's experience. Each parent had separate concerns. These were similar to concerns expressed by other couples. The mother worried about the effects of her irritability and the consequences of her outbursts on her children. The father was concerned about the mother's prognosis and her continued need for medication. He also was concerned about the long-term effects of her depression on the children.

In an individual session the 9-year-old son demonstrated that he was aware of his mother's depression. He indicated that he worked hard to get his mother to feel happy, but he became sad when she was irritable. He wondered why his mother got so mad and how she had become ill. He had no symptoms of psychiatric disorder at the time of assessment.

The family session provided an opportunity for the mother, father, and son to talk about the illness and their perceptions of it. The mother talked about how she felt when she was depressed. The father talked about his strategy for managing and stated that he remained hopeful. The son had the opportunity to ask two questions that had been on his mind: how does one get depressed, and what is the link between the stress of his sister's needs and his mother's illness?

The family's illness experience had been complicated by the care requirements of the older sister. Because of the mother's sense of guilt, an open discussion had been avoided. The intervention provided the occasion for the family to talk openly about the mother's illness and the factors that exacerbated it. In follow-up assessment by a separate rater, the parents reported that the intervention had been helpful in several areas, including educating their son about depression and related issues, helping them feel less stigmatized by the illness, educating them about risk and resilience, and increasing their understanding of their son's experience of the illness.

DISCUSSION

The findings from the first seven cases indicate that the intervention is safe for these families. These findings

meet Offord's first tenet for a preventive intervention program (11), that the intervention do more good than harm. Families participating in the intervention had suffered severe and long-standing affective illness. They had experienced marital and family difficulties but had not sought help for their children at the time of their enrollment. It was clear that regardless of the severity of the illness, all of the parents were worried about their children. The main concerns identified in assessment were addressed by the intervention. There was a reported decrease in the degree to which parents were upset by these specific concerns. Positive therapeutic alliances were developed with the parents, as measured by the Integrative Psychotherapy Alliance Scales. Parents reported a moderate to high level of satisfaction with the intervention. They were more satisfied with the information given about depression and child resilience, and attention to concerns about their children, than they were with issues related to the couples' communication and taking perspective.

Ten of 14 individuals, most of whom had a current or past psychiatric disorder, reported four or more changes in attitude or behavior regarding their children, their illness, and their spouses. Families noted the benefits of openly discussing the illness. The intervention gave them the tools to discuss issues that had not been discussed before. Several parents reported that they felt able to talk to their children about their illnesses for the first time and to explore how their children felt about the difficulties.

Although parents reported several changes in specific behaviors and attitudes related to the affective illness, overall marital satisfaction, as measured by the Dyadic Adjustment Scale, did not change. Couples often discussed long-standing issues in their marriages that were related to the affective illness and that had not been discussed before. As suggested by Gottman and Krokoff's findings (22), positive changes in marital satisfaction and other areas of couples and family functioning may become more evident as parents have time to examine the issues raised during the intervention.

We hypothesize that profound family misunderstanding of affective disorder contributes to a lack of recognition of distress in children. The intervention is designed to increase family perspective taking, provide ways of enhancing competence in the children, and increase understanding of the illness experience. It is expected that the process started by the intervention will continue.

The appropriate design for evaluation of this intervention is a long-term longitudinal study with a large sample. This design is necessary because the incidence in children of new cases of disorder that might be prevented by the intervention is low. Hence, the possibility of demonstrating effectiveness in a short-term study is limited. Random assignment of subjects to intervention and comparison groups and objective measures of impairment and understanding are essential components for evaluation.

A clinician-based intervention used by practitioners

who are the first and often only contact for individuals with affective disorders must include primary, secondary, and tertiary prevention. It follows that an appropriate assessment strategy to determine the effects of this intervention should be to examine these three levels of prevention outcome. Expected primary prevention would be a lower incidence of disorder in children of families receiving intervention than in families not receiving intervention. Secondary prevention would be recognition of warning signs of distress and prompt referral. Tertiary prevention would be the family's recognition of disorder, especially depression, in the children and appropriate help-seeking behavior. The current study does not establish the effectiveness of the intervention.

There are limits to the initial findings. The cohort size is small and heterogeneous. The individuals conducting the intervention and the assessment were blind to information about either process, but it was impossible for the assessors not to know which families had received the clinician-based intervention. This was not expected to have a large effect because the findings of objective attitude and behavior changes involved minimal inference. Nonetheless, it will be important to explore additional ways of measuring change. Finally, this report does not establish the safety and feasibility of the intervention for all families but only for those enrolled in the study. Safety and effectiveness should be evaluated on an ongoing basis.

CLINICAL IMPLICATIONS

An important consideration is the range of families for whom this intervention is appropriate. It is designed to be used by clinicians who are the first contact for families presenting with parental affective illness. The small cohort does not allow specific definition of families for whom the intervention is most appropriate. Families in the midst of a life crisis or acute episode of parental illness were excluded. We believe that such families need treatment rather than preventive intervention. Similarly, children presenting with acute depression need appropriate pharmacologic and psychotherapeutic intervention. However, a large number of families do not have these acute conditions and are appropriate for preventive intervention.

An extensive literature of epidemiologic surveys and pediatric practices reports a large number of serious, untreated child psychiatric disorders (23, 24). There is also a substantial literature to suggest that the children of depressed parents who become depressed do not receive treatment. Keller and colleagues (25) found that in 38 cases of major depression in the children of depressed parents, only seven received any intervention. In terms of tertiary prevention, investigators studying suicide and its prevention have indicated the need for aggressive treatment of childhood depression (26, 27). The question of how to reach families in which untreated childhood disorder may exist, or in which dis-

order may develop, is an important one. This study offers a conceptualization of an approach and demonstration of safety that suggests promise for reaching children who are at risk through increasing family members' understanding of what they have experienced and how they can move on with their lives.

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Depressive Illness Among Chemically Dependent Adolescents

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Objective: The purpose of this study was to investigate the prevalence and correlates of depression among adolescents being treated for chemical dependence. **Method:** Using the National Institute of Mental Health Diagnostic Interview Schedule, the authors interviewed 223 adolescents, aged 15–19 years, who were in residential treatment for alcohol or drug dependence diagnosed according to DSM-III-R criteria. Data on sociodemographic characteristics, school and social performance, past history, family composition, familial alcohol and drug abuse, and previous victimization of the subjects were also gathered. **Results:** Fifty-four (24.7%) of the subjects met the DSM-III-R criteria for depression. Very few of the traditional correlates of depression discriminated depressed from nondepressed subjects, suggesting that the presence of chemical dependence overrides other predictors of depression. Only female gender, paternal psychopathology, and victimization (physical abuse, sexual abuse) emerged as important variables associated with depression. However, subjects whose onset of depression preceded their chemical dependence had different characteristics from those whose depression began after their chemical dependence. **Conclusions:** The prevalence of depressive illness in these chemically dependent adolescents was approximately three times that reported for nonreferred groups of similar age. This high rate of depression reflects the contributions of two distinct groups—those with primary depression and those with depression subsequent to chemical dependence—whose characteristics differed, suggesting the possibility of two pathologic processes, similar in manifestation but with different associated features and possibly with distinct etiologies. Confirmation of these findings in further research could indicate that the two forms of depression may require different treatment approaches.

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Epidemiologic studies have confirmed clinical reports linking psychiatric morbidity with substance abuse in adult populations (1–4). Interest in comorbidity is sparked by the recognition that the presence or absence of psychiatric disorder may be an important means of subtyping substance abusers and could lead to refinement of the classification of both alcohol and drug abuse. Furthermore, the division of substance-abusing individuals into subgroups with and without additional psychiatric morbidity could elucidate different etiologic factors in the development of substance abuse and provide important information for group-specific treatment approaches. The connection of sub-

stance abuse and psychiatric illness is now well established in both referred and community adult populations. However, relatively little is known about the co-occurrence of psychiatric morbidity and substance abuse in adolescents. Although several investigators have reported the association of psychiatric symptoms with substance abuse in teen-age subjects, it is not clear to what extent such psychiatric symptoms reflect an actual diagnostic entity (5–7). In a previous study of the co-occurrence of depressive illness and substance abuse in 424 college freshmen (8), we found that alcohol abuse was associated with major depressive disorder only, while drug abuse was associated with major depressive disorder and other DSM-III diagnoses as well. However, the relatively low frequency of these psychiatric diagnoses in the college population made it difficult to examine specific correlates of the observed associations.

A study of the possible interconnection of substance abuse and psychiatric illness during adolescence could have important implications for prevention and treatment. Adolescence is a pivotal stage of human development, posing simultaneous challenges in the cognitive, psychological, and social spheres. If mastery of these

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challenges is impaired by psychiatric illness, deleterious consequences may be more likely to occur than if psychopathology begins in adulthood. Focusing study on the adolescent rather than the adult may facilitate the identification of risk factors that are more proximal to the onset of psychiatric illness. In addition, the temporal sequence of chemical dependence and psychiatric morbidity may be easier to determine in adolescence, when the two have not yet become so intertwined that it is nearly impossible to determine which is primary.

In this study we examined the prevalence and correlates of major depression among adolescents who were receiving inpatient treatment for dependence on alcohol, drugs, or both. Depression was specifically chosen for study because of its reported association with substance abuse in adulthood and because epidemiologic data have indicated a progressive increase in the incidence of depression during adolescence among cohorts born after 1935 (9, 10). These are the birth cohorts that have also experienced increased use of alcohol and, more recently, drugs. In addition, we chose depression because its subjectively painful symptoms could trigger repeated self-medication, leading to substance abuse. Conversely, depression could also result from the social difficulties caused by heavy use of alcohol and drugs or by the action of drugs that depress the CNS. By selecting a study group of chemically dependent adolescents, we removed substance abuse as a potential confounding factor, permitting a less obscured examination of other possible etiologic variables in the development of depression.

The purpose of this study was threefold: to assess the prevalence of depression diagnosed according to *DSM-III-R* in a group of adolescents undergoing treatment for chemical dependence, to examine potential correlates of depression in this population, and to investigate, among those subjects who met the criteria for depression, whether depression preceded or followed chemical dependence.

METHOD

The 223 study subjects (168 male and 55 female) were drawn from seven of the eight residential treatment centers for substance-abusing adolescents funded by the Massachusetts Department of Public Health, which underwrote the cost of approximately half of the hospital beds. Funding for most of the other patients came from state revenues (Medicaid, the Department of Social Services, or the Department of Youth Services); only a few subjects were covered by private insurance. The eighth treatment center chose not to participate in the study. The seven participating facilities contained a representative population of adolescents whose treatment was supported by public funds.

The treatment sites drew patients from the entire state. Three sites treated both male and female patients, three accepted only male patients, and one accepted only female patients. The length of treatment ranged

from 3 to 18 months. All treatment programs were modeled on the Alcoholics Anonymous/Narcotics Anonymous 12-step program, which focuses on group discussions, assigned tasks, and well-defined, graded levels of responsibility as the core of treatment. Academic work was also compulsory for subjects who had not finished high school.

To be eligible for participation in the study, subjects had to be 15–19 years of age, meet the *DSM-III-R* criteria for dependence on alcohol, drugs, or both, and sign an informed consent form. For subjects under age 18 who were not legally empowered to make their own health care decisions, signed parental consent was also obtained. The study was approved by the institutional review boards of the Harvard School of Public Health and the Massachusetts Department of Public Health and by the directors of the treatment centers. Eligible subjects were enrolled in the study between the second and fourth weeks of treatment. We compared the age, sex, and race distributions of enrolled subjects with those of subjects who chose not to participate and found that there were no differences between the two groups. This suggests that the enrolled subjects were representative of young patients entering treatment at the sites.

Information leading to the establishment of psychiatric diagnoses was obtained with the National Institute of Mental Health Diagnostic Interview Schedule (DIS) (11), version III-R, administered by research assistants trained in the use of this instrument. The research assistants were college graduates who had previous experience working with adolescents. Training in the use of the DIS consisted of approximately 50 hours of classroom instruction, trial interviews, homework assignments, field experience under supervision, and, finally, training interviews with adolescents who were not entered in the study. Staff meetings were held regularly to resolve any ambiguities that had been encountered during the interviews and to ensure that there had not been any drift from the established protocol.

The DIS was specifically designed for persons aged 18 and over. However, we had previously used this interview with 16- and 17-year-olds and found that respondents understood the questions well and had no difficulty providing the required information (12). Similarly, our experience with the current study group indicates that the DIS works equally well with persons as young as 15. The only diagnosis that could not be established in our group of subjects was that of antisocial personality disorder, which can be ascertained only for persons over the age of 18.

We obtained data on the subjects' background characteristics, family composition, school and social performance, work history, familial substance use, and history of victimization by means of the Family and Social History Interview, a structured interview based on the Winters Adolescent Diagnostic Interview (13) but substantially expanded and changed to meet the needs of this study.

Administration of the DIS and the Family and Social

TABLE 1. Characteristics of Adolescent Subjects With Chemical Dependence

Characteristic	Male Subjects (N=168) ^a		Female Subjects (N=55) ^a		All Subjects (N=223) ^a		Analysis	
	N	%	N	%	N	%	χ^2 (df=1)	p
Nonwhite race	25	14.9	9	16.4	34	15.2	0.1	0.79
Retained in same grade 2 or more years	77	45.8	8	14.6	85	38.1	17.2	0.001
Family ever received welfare	89	54.9	35	68.6	124	58.2	3.0	0.08
Perceived family socioeconomic status below average	26	15.8	7	13.2	33	15.2	0.2	0.64
Father deceased	12	7.8	3	5.9	15	7.3	0.2	0.64
Mother deceased	2	1.3	3	6.0	5	2.4	3.6	0.06
Lived with parent(s) just prior to treatment	132	78.6	51	92.7	183	82.1	5.6	0.02
Meets <i>DSM-III-R</i> criteria								
Alcohol dependence only	6	3.6	7	12.7	13	5.8	6.3	0.01
Drug dependence only	9	5.4	5	9.1	14	6.3	1.0	0.32
Both alcohol and drug dependence	150	89.3	42	76.4	192	86.1	5.8	0.02
Depressive illness	28	16.9	26	48.2	54	24.7	21.5	0.001

^aNumber of subjects on which percents for individual items are based varies slightly because of missing data on some items for some subjects.

History Interview took about 2 hours. Data obtained by the DIS were scored on a personal computer with the use of a scoring program we developed to generate a profile of *DSM-III-R* axis I diagnoses for individual subjects as soon as their DIS data are entered in the computer. The diagnoses generated with the personal computer data scoring program were identical to those generated by the standard mainframe scoring program. (Information on the personal computer scoring algorithm is available from the first author on request.)

Data were analyzed with an SAS program (14). Odds ratios and 95% confidence intervals were calculated for male and female subjects separately to assess the association of depression with several potential correlates. Summary estimates for the total group were also calculated, controlling for gender, by the Mantel-Haenszel summary odds ratio (15). The odds ratio quantifies the association of two variables. Odds ratios equal to 1 indicate that the variables are independent of each other, whereas those above and below 1 indicate positive and negative associations, respectively. The greater the departure from 1, the null value, the stronger the association.

RESULTS

The mean age of the subjects was 16.5 years (SD=1.1). Table 1 shows other sociodemographic characteristics of the study group, which overall was representative of a disadvantaged group. Families of more than half of the subjects had received some form of welfare assistance (Aid to Families With Dependent Children, food stamps, Medicaid, fuel assistance, subsidized housing). More than one-third of the subjects had been retained in the same school grade for 2 or more years. The education deficit was particularly pronounced among the male subjects, who were three times as likely as the female subjects to be substantially behind in school. The proportion of nonwhite subjects in the study (15.2%) was only slightly higher than the

proportion of the minority population of Massachusetts (12%) reported by the 1990 census.

All subjects met the *DSM-III-R* criteria for alcohol or drug dependence, and 86.1% met the criteria for both (table 1). A total of 54 subjects met the *DSM-III-R* criteria for major depression. The lifetime prevalence of depression was 24.7%, with the prevalence among females more than 2.5 times the prevalence among males—a highly significant difference. The prevalence of depressive illness among these chemically dependent adolescents was between two and four times the prevalence that has been found in clinical samples of comparable age in studies that have used the DIS to diagnose psychopathology. In our previous study of college students aged 16–18 years (8), we found that 8.2% met established criteria for major depressive disorder. Although the prevalence of depression among the college students was only one-third as high as that in the present study, the ratio of depressed females to depressed males (2.5:1) was similar to that in the present study. Furthermore, in a recent report, Burke et al. (16) applied life table survival analysis techniques to the Epidemiologic Catchment Area (ECA) study data to estimate the prevalence of depressive illness in a community sample at various ages. The authors found that 4.4% of the females and 2.4% of the males had experienced at least one episode of depressive illness before the age of 20. Despite the variation in the estimates of the prevalence of depression, the twofold greater risk for females was consistent among the college students, the ECA sample, and the adolescents in this study.

Apart from gender, a number of other sociodemographic characteristics have been identified as possible correlates of depression (17). Among these are living apart from natural parents, school failure, low socioeconomic status, parental psychopathology, and victimization (18–22). To test whether these and similar factors increased the risk of depression in a chemically dependent population, we assessed the association of selected sociodemographic, family history, and victimization characteristics with depression.

TABLE 2. Association of Depression and Sociodemographic Characteristics Among Adolescent Subjects With Chemical Dependence

Variable	Male Subjects (N=168) ^a				Female Subjects (N=55) ^a				All Subjects (N=223) ^a			
	N	%	Odds Ratio	95% Confidence Interval	N	%	Odds Ratio	95% Confidence Interval	N	%	Odds Ratio ^b	95% Confidence Interval
White race	142	85.5	1.0	0.3–3.1	45	83.3	0.5	0.1–2.2	187	84.8	0.8	0.3–1.8
Firstborn child	71	45.2	0.7	0.3–1.6	32	59.3	1.6	0.6–5.0	103	48.8	0.9	0.5–1.8
Retained in same grade for 2 or more years	75	45.2	1.8	0.8–4.1	8	14.8	0.6	0.1–2.8	83	37.7	1.4	0.7–2.8
Family ever received welfare	88	55.0	0.7	0.3–1.6	35	68.6	0.6	0.2–1.9	123	63.1	0.7	0.3–1.3
Perceived family socioeconomic status below average	26	16.0	2.3	0.8–6.1	7	13.5	1.5	0.3–7.6	33	19.5	2.0	0.9–4.6

^aNumber of subjects on which percents for individual items are based varies slightly because of missing data on some items for some subjects.

^bMantel-Haenszel summary odds ratio, controlled for gender.

TABLE 3. Association of Depression and Familial History of Substance Use and Psychopathology Among Adolescent Subjects With Chemical Dependence

Variable	Male Subjects (N=168) ^a				Female Subjects (N=55) ^a				All Subjects (N=223) ^a			
	N	%	Odds Ratio	95% Confidence Interval	N	%	Odds Ratio	95% Confidence Interval	N	%	Odds Ratio ^b	95% Confidence Interval
Alcohol problem												
Mother	49	31.0	0.6	0.2–1.5	19	36.5	0.7	0.2–2.4	68	32.3	0.6	0.3–1.3
Father	88	60.3	1.2	0.5–2.7	33	67.4	0.7	0.2–2.4	121	62.1	1.0	0.5–2.0
Siblings	44	26.5	2.1	0.9–4.8	15	27.8	0.9	0.3–3.0	59	26.8	1.5	0.8–3.1
Drug problem												
Mother	30	18.9	0.1	0.0–1.0	16	32.0	1.6	0.5–5.4	46	22.0	0.6	0.2–1.5
Father	61	40.4	0.4	0.1–1.0	19	42.2	1.2	0.4–4.0	80	40.8	0.6	0.3–1.2
Siblings	41	24.7	1.9	0.8–4.6	12	22.2	1.1	0.3–4.0	53	24.1	1.6	0.8–3.3
Psychological problem												
Mother	48	31.0	1.1	0.5–2.8	31	59.6	1.6	0.5–5.0	79	38.2	1.3	0.6–2.6
Father	31	22.8	1.8	0.6–4.8	14	34.2	3.6	0.9–14.6	45	25.4	2.3	1.0–5.1
Siblings	61	36.8	0.8	0.3–1.9	24	44.4	1.5	0.5–4.6	85	38.6	1.0	0.5–2.0

^aNumber of subjects on which percents for individual items are based varies slightly because of missing data on some items for some subjects.

^bMantel-Haenszel summary odds ratio, controlled for gender.

None of the sociodemographic characteristics we studied had a statistically significant association with depressive illness (table 2). Perception of low socioeconomic status was the only variable that indicated even a modest elevation in the risk of depression for both sexes. Most of the other sociodemographic variables had a paradoxically different relationship with depression for the male and female subjects: variables that were positively associated with depression among females were negatively associated among males, and vice versa. However, because all associations were very close to the null value, and none was statistically significant, this paradoxical effect probably represents random variation. Overall, our examination of sociodemographic variables and depression in this study group does not support the findings of previous studies.

Table 3 presents the data on the association of depression with familial alcohol abuse, familial drug abuse, and reported history of emotional or psychological problems in the subjects' first-degree relatives. Parental alcohol abuse has long been associated with depressive symptoms in children, and therefore familial alcohol and drug abuse were assessed for a possible link with depression. Similarly, parents' psychopathology,

especially depressive illness, has also been reported to increase the risk of depression in their children (23). We obtained histories of familial alcohol and drug abuse and psychopathology by interviewing the subjects rather than by direct examination of parents and siblings. Subjects were asked, "Did your (mother/father/siblings) ever have a psychological, emotional, or mental problem?"

Alcohol abuse by the mother was reported by about one-third of the subjects, alcohol abuse by the father was reported by almost two-thirds of the subjects, and alcohol abuse by siblings was reported by about one-fourth of the subjects (table 3). Drug abuse by the mother was reported by almost one-fourth of the subjects, drug abuse by the father by almost half, and drug abuse by siblings by nearly one-fourth. Although fathers were more likely than mothers to have histories of alcohol or drug abuse, they were less likely to be identified as having a psychological problem. With the exception of paternal psychopathology, the high frequency of familial substance abuse and psychopathology did not consistently elevate the risk of depressive illness.

Several investigations have reported an association

TABLE 4. Association of Depression and History of Victimization Among Adolescent Subjects With Chemical Dependence

Variable	Male Subjects (N=168) ^a				Female Subjects (N=55) ^a				All Subjects (N=223) ^a			
	N	%	Odds Ratio	95% Confidence Interval	N	%	Odds Ratio	95% Confidence Interval	N	%	Odds Ratio ^b	95% Confidence Interval
Victim of physical abuse	47	34.3	1.5	0.6–4.0	24	55.8	5.6	1.5–21.1	71	39.4	2.4	1.2–5.1
Child abuse report filed	28	17.5	1.0	0.4–3.0	21	43.8	3.4	1.0–11.3	49	23.5	1.8	0.8–3.8
Victim of sexual abuse	14	8.5	1.4	0.4–5.3	41	75.9	2.6	0.7–9.8	55	25.1	1.9	0.8–4.9
Removed from home by authorities	30	19.1	0.7	0.2–2.3	21	41.2	1.4	0.5–4.4	51	24.5	1.0	0.5–2.3

^aNumber of subjects on which percents for individual items are based varies slightly because of missing data on some items for some subjects.

^bMantel-Haenszel summary odds ratio, controlled for gender.

between child abuse/neglect and subsequent depressive manifestations or suicidal behavior (22–25). Because of this reported link, we examined whether prior victimization was related to depressive illness. Victimization was assessed by asking subjects four separate questions: whether they had ever been physically abused, whether a report of child abuse/neglect had ever been filed on their or their siblings' behalf, whether they had ever been sexually abused, and whether they had ever been removed from their home by state authorities. Table 4 shows that nearly all indicators of victimization increased the risk of depression, irrespective of gender. Of the four types of victimization, physical abuse was associated with the highest risk of depression; its association with depression was statistically significant for the female subjects ($\chi^2=6.2$, $df=1$, $p=0.01$) and for the entire study group when gender was controlled ($\chi^2=8.8$, $df=1$, $p<0.01$). Compared to the nondepressed subjects, depressed male subjects were 1.5 times more likely and depressed female subjects were 5.6 times more likely to have experienced physical abuse. Sexual abuse, which was endemic among the female subjects, more than doubled the risk of depression; sexual abuse of the male subjects increased their risk of depression by only 40%. However, the increased risk of depression was not great enough to be statistically significant for either sex. Removal of the subject from the home by authorities was a risk factor for depression among the female subjects only.

Of the three categories of risk factors—sociodemographic, familial substance abuse and psychopathology, and victimization—only victimization appears to have been a consistent risk factor for depressive illness in this group of chemically dependent adolescents. Both gender and paternal psychopathology continued to be significantly related to depressive illness at the $p<0.05$ level. However, after adjusting for these variables, we found that history of physical abuse fell just short of statistical significance (odds ratio=2.0; 95% confidence interval=0.9–5.1). The independent association between physical abuse and depression was partly due to the link between gender, paternal psychopathology, and depression. The three variables that were independently associated with depression for the whole group of subjects (gender, paternal psychopathology, and physical abuse) were examined simultaneously in a

logistic regression model predicting depression, and although all three continued to show an association with depression the association was significant only for the first two.

Because depressed and nondepressed adolescents appear to be similar on many variables, we further assessed whether the depressed subjects had histories of more severe substance abuse by comparing the mean ages at which the two subgroups of subjects became chemically dependent and the number of substances they had used. Overall, the depressed subjects developed chemical dependence at an earlier age (mean=11.8 years, $SD=2.3$) than did the nondepressed subjects (12.7 years, $SD=1.9$), and the depressed subjects used a slightly higher number of substances (mean=4.1, $SD=2.3$, versus mean=3.7, $SD=2.0$). The younger age at the development of chemical dependence was statistically significant only for the male subjects (mean=11.5 years, $SD=2.1$, versus mean=12.6 years, $SD=2.1$; $t=2.4$, $df=166$, $p=0.02$), and the larger number of substances used was significant only for the female subjects (mean=4.1, $SD=2.6$, versus mean=2.9, $SD=1.9$; $t=1.96$, $df=53$, $p=0.05$).

The temporal sequence of depression and severe substance abuse in adolescence is an area that has not been examined previously, and it is one that poses inherent methodologic difficulties. A major problem is determining when an individual passes from a nonpathologic state to a pathologic one. Specifically, it is difficult to differentiate the moment at which symptoms become a syndrome. To examine the sequence of chemical dependence and depression among the 54 depressed subjects, we compared the ages at which each subject first met established criteria for depressive illness and for chemical dependence. Three time patterns of comorbidity were possible: depression followed by chemical dependence, depression preceded by chemical dependence, and both occurring at approximately the same time. Because we adhered to stringent *DSM-III-R* criteria for diagnosis, we cannot exclude the possibility that prodromal characteristics—such as depressive symptoms or dysphoria in the case of depression or substantial alcohol or drug use in the case of chemical dependence—may have occurred before the age at which full *DSM-III-R* criteria for the two disorders were met. Onset of depression was designated as the age at which a

TABLE 5. Temporal Sequence of Depression and Chemical Dependence Among 51 Depressed Adolescent Subjects

Variable	Depressed Subjects					
	Male		Female		Total	
	N	%	N	%	N	%
Depression occurred first	8	44.4	10	55.6	18	35.2
Chemical dependence occurred first	15	68.2	7	31.8	22	43.1
Both occurred at same time	3	27.3	8	72.7	11	21.6
Total	26	51.0	25	49.0	51	100.0

subject met all criteria for depressive illness. Similarly, onset of alcohol or drug dependence was defined as the earliest age at which all criteria were met.

Table 5 shows the temporal sequence of depression and chemical dependence for 51 of the 54 depressed subjects. We were not able to establish the temporal sequence for three subjects and thus did not include them. The male subjects were twice as likely as the female subjects to have the onset of depression follow chemical dependence, whereas females were more likely to have depression as the primary disorder or to have it co-occur with chemical dependence. Due to the small subgroup sizes in this analysis, the difference between males and females fell just short of statistical significance ($\chi^2=5.37$, $df=2$, $p=0.08$). Regardless of whether depression preceded or followed chemical dependence, the female subjects became depressed at an earlier age. The greatest difference between male and female subjects in age at onset of depression was among those whose depression preceded chemical dependence (2.6 years), but the difference was evident in a more muted form (0.6 years) even among those whose chemical dependence occurred first.

Because the sequence pattern of depression and chemical dependence differed for the two sexes, we examined other variables to determine whether any were associated with a specific pattern of comorbidity. The 51 depressed subjects were divided into three subgroups designated by the patterns of the temporal sequence of depression and chemical dependence. The 18 subjects who experienced depression first were compared to the 22 subjects whose depression followed chemical dependence with respect to the sociodemographic, familial, and victimization variables shown in tables 2-4. The 11 subjects for whom depression occurred at the same time as chemical dependence were eliminated from this analysis. Odds ratios of 1.8 or more were deemed to suggest an association with a specific pattern of comorbidity. Table 6 lists the variables associated with each of the two sequences of comorbidity. Subjects for whom depression was the primary disorder had characteristics that have traditionally been considered correlates of depressive symptoms in adolescence, namely, female gender, emotional/psychiatric problems in a parent, and victimization. Conversely, substance abuse by first-degree relatives and poor academic performance were the salient characteristics of

TABLE 6. Variables That Differentiated Temporal Sequences of Depression and Chemical Dependence Among 51 Depressed Adolescent Subjects

Variable	Odds Ratio
Subjects with onset of depression before onset of chemical dependence (N=18)	
Female gender	2.8
Psychological problem in mother	2.2
Drug problem in father	2.3
Child abuse report filed	3.4
Victim of sexual abuse	1.8
Subjects with onset of depression after onset of chemical dependence (N=22)	
Retained in same grade for 2 or more years	4.2
Alcohol problem in father	2.5
Alcohol problem in mother	2.9
Alcohol problem in siblings	4.2
Drug problem in siblings	5.5

the subjects whose depression developed only after chemical dependence.

DISCUSSION

The findings of this study suggest that among chemically dependent adolescents, depressive illness may consist of an admixture of two forms. One form, affecting a relatively small number, is primary depression with associated features that are known correlates of affective disorder. The other form, present in a larger number of subjects, is depression secondary to chemical dependence with associated features characteristic of severe substance abuse. Although these two forms taken together constituted an extremely high occurrence of depression overall (24.7%), if one considers only primary depression, the prevalence diminishes to only 8.1% (18 of 223 subjects). This rate of primary depression is similar to the 8.2% found in our study of college students (8) and to the 8.6% reported by Kandel and Davies (26) in their study of severe depressive symptoms in a group of nonreferred adolescents. The concordance of these three rates could imply that the excessive rate of depressive illness seen in the present study represents two separate pathologic processes, with substance abuse as the etiologic factor for secondary depression. This explanation is further supported by the lack of differentiation of depressed and nondepressed subjects with respect to the traditional risk factors for depression. If there are two forms of depression, each with separate associated characteristics, when depressed subjects are compared to nondepressed subjects, the known risk characteristics for depression will be muted.

The obscuring of differences between depressed and nondepressed subjects was evident in this study. Only a few variables—female gender, paternal psychopathology, and a history of physical abuse—independently emerged as statistically significant in differentiating subjects with and without depression. In addition,

other components of victimization—sexual abuse and a history of a report of child abuse—also increased the risk of depression but fell short of statistical significance. We propose that victimization is not simply a confounding factor in the relation between gender and primary depression, since the association between victimization and depression remained strong even when gender was controlled. The independent effect of victimization suggests two possible explanations. Children exposed to abuse may incorporate the negative opinions conveyed by the abusers and are thus likely to have diminished self-esteem. In addition, if the abuser is a parent or primary caretaker, the child is denied the opportunity for solace, which is necessary in order to develop appropriate adaptive mechanisms. Low self-esteem and the inability to respond to adverse events are suspected components of depressive illness. Furthermore, if abuse necessitates the removal of the child from the home, disruptions of bonding may occur, making the child more vulnerable to subsequent psychopathology.

Data from this study have shown that among adolescents undergoing treatment for chemical dependence, the rate of depression is approximately three times that among persons of similar age who have not been referred for medical treatment. Part of this high rate may be the result of Berkson's bias (27). This bias produces an overestimate of comorbidity, since persons who enter treatment are more likely to do so if they suffer from more than one condition. Therefore, clinical samples will have higher rates of comorbidity than samples drawn from the community. The extent to which Berkson's bias operated in this study cannot be quantified, but it is perhaps less than in other clinical samples because a sizable proportion of the adolescents studied did not choose to obtain treatment, having been remanded to the treatment sites by court orders.

Despite the possibility of an overestimate of the prevalence of depression, the findings suggestive of two forms of clinical depression open a challenging area of investigation, which could possibly lead to a refinement of disease classification and have important implications for treatment. Patients with primary depression who are chemically dependent might well profit from treatment directed at their depression rather than at their chemical dependence. Conversely, those who become depressed after they have developed chemical dependence might show greatest improvement when treatment is targeted at their alcohol and drug abuse rather than at their depression.

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Resident Physician Substance Use, by Specialty

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***Objective:** This study compares substance use by medical specialty among resident physicians. **Method:** The authors estimated the prevalence of substance use of 11 medical specialties from a national sample of 1,754 U.S. resident physicians. **Results:** Emergency medicine and psychiatry residents showed higher rates of substance use than residents in other specialties. Emergency medicine residents reported more current use of cocaine and marijuana, and psychiatry residents reported more current use of benzodiazepines and marijuana. Contrary to recent concerns, anesthesiology residents did not have high rates of substance use. Family/general practice, internal medicine, and obstetrics/gynecology were not among the higher or lower use groups for most substances. Surgeons had lower rates of substance use except for alcohol. Pediatric and pathology residents were least likely to be substance users. **Conclusions:** The authors' previous research indicates that residents overall have lower rates of substance use than their age peers in society. Yet resident substance use patterns do differ by specialty. Residents in some specialties are more likely to use specific classes of drugs, to use a greater number of drug classes, and to be daily users of alcohol or cigarettes.*

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The ready availability of dependence-producing substances poses an occupational risk to physicians and other health professionals, but this risk does not appear to be evenly distributed among the medical specialties. Data from drug treatment programs, medical licensing boards, and surveys of physicians suggest that members of certain specialties are at greater risk of substance use.

Studies of treated populations include Bissell et al.'s follow-up of 98 male and 95 female physician members of Alcoholics Anonymous (1, 2). Using known specialty distributions for U.S. physicians, Bissell et al. found male and female psychiatrists to be overrepresented and observed a similar tendency for female physicians in emergency medicine. Surgical specialties were underrepresented. Morse et al. (3) reviewed 73 chemically dependent physicians treated at the Mayo Clinic and found that family/general practitioners and, to a lesser

extent, anesthesiologists were overrepresented. Talbott et al. (4) described 1,000 physicians treated at Smyrna, Ga., 92% of whom had a primary diagnosis of chemical dependence. Anesthesiologists, thoracic surgeons, emergency medicine practitioners, plastic surgeons, and family/general practitioners were overrepresented. Pediatricians and pathologists were underrepresented.

State licensing boards are another source of data on physician substance abuse. In a study of 34 physicians disciplined by the Oregon board, Shore (5) reported that psychiatrists were overrepresented when compared to the expected rate among registered physicians in that state. Ikeda and Pelton (6) studied 247 physicians enrolled in the California Diversion Program; over 90% were being treated for substance abuse. Three specialties—anesthesiology, emergency medicine, and family/general practice—were overrepresented.

Survey researchers have also investigated drug use in medical specialties. Sethi and Manchanda (7) interviewed 240 resident physicians in India but did not compare drug use rates by specialty. McAuliffe et al.'s questionnaire survey (8) of 489 physicians selected from the Massachusetts Medical Society membership found psychiatrists to have much higher rates of use for all types of substances, followed by anesthesiologists. Maddux et al. (9) found psychiatry residents at a Texas medical center more likely than residents in other specialties to report benzodiazepine use in the past year. Myers and Weiss (10), in a survey of 1,805 interns and

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residents in Ontario, Canada, found that anesthesiology and psychiatry ranked among the first five of 11 specialties for each of three patterns of substance use. Community health residents were least likely to use substances, followed by residents in emergency medicine, surgery, and pediatrics. Moore et al. (11) followed 1,014 graduates of Johns Hopkins School of Medicine and found no statistically significant differences in rates of alcohol abuse in the major specialties.

In the preceding studies, physicians in anesthesiology, emergency medicine, family/general practice, and psychiatry were found to be at higher risk of substance use or abuse than physicians in other specialties, but these findings were not consistent across the various studies. This raises the question of possible biases due to inadequate or nonrepresentative samples, especially when studies are confined to physicians in a single medical center, state, or treatment program.

To further explore drug use differences by medical specialty, we examined data from a national survey of U.S. resident physicians (12). The survey provided data on drug use patterns in 11 medical specialties. The aim was to identify those specialties which were at greatest risk of 1) unsupervised use of specific drug classes or types, 2) multiple drug use, and 3) daily substance use, as well as 4) legitimate use of controlled substances under the supervision of another physician. Background variables were examined to determine if observed differences in substance use patterns might be explained by factors other than specialty status.

METHOD

The study sample was drawn from the American Medical Association physician master file, which is considered the most comprehensive listing of U.S. physicians available. The sampling frame consisted of 15,814 U.S. physicians in their third year of residency training who had graduated from medical school in 1984. The 3,000 subjects were a stratified random sample selected to ensure that their distribution by major specialty reflected that of the master file. The 11 specialties were anesthesiology, emergency medicine, family/general practice, internal medicine (including subspecialties), obstetrics/gynecology, pathology, pediatrics, psychiatry, radiology, surgery (including subspecialties), and a category for those who were in another specialty or who were undecided.

In the spring of 1987, each subject was sent an anonymous questionnaire, a cover letter with a \$1 incentive, and a response postcard (with subject identification number) to be returned separately. The eight-page, multiple-choice questionnaire was designed for an optical mark reader and took 15–25 minutes to complete. Up to two follow-up questionnaires were sent to subjects whose postcards were not returned.

Questions covered demographic characteristics, medical specialty, work activities, and drug use. Respondents were asked how frequently they had used each of 11 types

of drugs in their lifetime, in the past year, and in the past 30 days. Substance categories included cigarettes, alcohol, marijuana, cocaine, LSD, other psychedelic drugs, heroin, and prescription drug types including amphetamines, barbiturates, benzodiazepines, and opiates other than heroin. Questions on prescription drugs included the phrase "without a doctor telling you to use them." The questions were based on the National Institute on Drug Abuse's Monitoring the Future study at the University of Michigan Institute for Social Research in Ann Arbor in order to allow comparison with a sample of similar age (13). Drug use questions had been field tested on medical students in earlier pilot work (14, 15).

The overall response rate was 60% (N=1,785). Of these, 1,754 indicated current specialty and were used for this analysis. Distribution of specialties among respondents reflected the actual distribution of residents in specialty training programs for the year of the survey (16). The drug use prevalence rate of each specialty was compared to that of all others combined. Statistical significance was evaluated by using the chi-square test for stratified samples (one degree of freedom) and 95% confidence intervals.

RESULTS

Are Residents in Some Specialties More Likely to Use Specific Types of Substances?

The proportion of residents in each specialty who had ever used 10 of the 11 substances in their lifetime appears in table 1. Heroin users were too few to draw firm conclusions regarding specialty differences, and therefore the data are not shown.

Use of nonprescribed substances. Little variation was observed across specialties in relative ranking of the legal and illicit substances used. This trend held for both lifetime (table 1) and past year (figure 1) substance use. Residents in all specialties reported alcohol as the most widely used substance. Over 90% of residents in each specialty reported having used alcohol in their lifetime and in the past year, and more than 80% in each specialty reported use in the past month. Among the nonprescribed substances, marijuana was the second most frequently used substance for all the specialties, cigarettes were third, cocaine fourth, and psychedelics fifth (figure 1).

The following five specialties had substance use rates close to the mean for all residents: anesthesiology, internal medicine with its subspecialties, surgery with its subspecialties, radiology, and those signifying "other." Psychiatry and emergency medicine residents showed higher rates of drug use than did other specialties. Psychiatry residents had the highest rates for lifetime-ever use of marijuana (prevalence=80.7%, 95% confidence interval=72–89, $p=0.002$), cigarettes (prevalence=65.5%, 95% confidence interval=55–76, $p=0.008$), cocaine (prevalence=45.5%, 95% confidence interval=35–56, $p=0.001$), LSD (prevalence=30.7%, 95% confidence interval=21–40, $p=0.0001$), and other psychedelic sub-

TABLE 1. Lifetime Use of Psychoactive Substances Reported by 1,754 Resident Physicians, by Specialty

Specialty	Alcohol		Marijuana		Cigarettes		Cocaine		Benzodiazepines		Amphetamines	
	%	CI ^a	%	CI ^a	%	CI ^a	%	CI ^a	%	CI ^a	%	CI ^a
Anesthesiology	98.3	96-101	68.7	60-77	59.1	50-68	34.5	26-43	22.6	15-30	29.6	21-38 ^d
Emergency medicine	100		79.6	68-91 ^d	55.1	41-69	38.0	25-52	32.0	19-45	26.0	14-38
Family/general practice	96.5	94-99	59.6	54-66 ^d	49.2	43-55	17.6	13-22 ^d	20.8	16-26	14.5	10-19 ^d
Internal medicine	97.4	96-99	64.3	60-69	49.6	45-54	28.7	25-33	23.6	20-27	20.3	17-24
Obstetrics/gynecology	98.2	96-101	62.0	53-71	42.7	33-52	26.6	18-35	19.3	12-27	23.9	16-32
Pathology	100		62.7	50-76	58.8	45-72	19.6	9-31	19.6	9-31	27.5	15-40
Pediatrics	93.8	90-97 ^d	55.9	49-63 ^d	47.4	40-55	24.7	18-31	16.4	11-22 ^d	19.0	13-25
Psychiatry	97.7	95-101	80.7	72-89 ^d	65.5	55-76 ^d	45.5	35-56 ^d	50.0	40-60 ^d	31.8	22-42 ^d
Radiology	95.8	92-100	74.7	66-84	57.0	47-67	37.9	28-48	30.5	21-40	20.0	12-28
Surgery	98.9	98-100	66.2	60-72	50.2	44-56	35.1	29-41	16.4	12-21 ^d	18.3	14-23
Undecided/other	100		71.4	61-82	53.6	42-65	28.6	18-39	25.7	16-36	24.6	15-35
All trainees	97.3	97-98	65.1	63-67	51.5	49-54	29.2	27-31	22.7	21-25	20.8	19-23

^a95% confidence interval.^bOther than heroin.^cNot including LSD.^dSignificant difference compared to all other trainees for that substance ($p \leq 0.05$, chi-square analysis).

stances (prevalence=30.7%, 95% confidence interval=21-40, $p=0.0001$). Psychiatry also had the highest percentage of marijuana users in the past year (prevalence=34.1%, 95% confidence interval=24-44, $p=0.0001$). Emergency medicine had the highest rate of cocaine use in the past month (prevalence=8.0%, 95% confidence interval=1-16) and the past year (prevalence=14.0%, 95% confidence interval=4-24) and high use rates in the past year for marijuana (prevalence=28.6%, 95% confidence interval=16-41, $p=0.03$) and cigarettes (prevalence=16.3%, 95% confidence interval=6-27).

Specialties with lower rates of nonprescribed substance use included family/general practice, obstetrics/gynecology, pediatrics, and pathology. Family/general practice residents had the lowest rate of ever having used cocaine (prevalence=17.6%, 95% confidence interval=13-22, $p=0.0001$) and psychedelic substances (other than LSD) in their lifetime. Obstetrics/gynecology had the lowest lifetime-ever rate of cigarette use. Pediatric residents had the lowest lifetime-ever use of marijuana (prevalence=55.9%, 95% confidence interval=49-63, $p=0.006$) and alcohol (prevalence=93.8%, 95% confidence interval=90-97, $p=0.002$). Pathology residents dropped from the third highest rate of lifetime-ever cigarette use to the lowest rate in the past year and past month. Pathology residents also reported the lowest rate of past year use of cocaine and marijuana.

Unsupervised use of prescription drugs. Little cross-specialty variation was also observed in relative ranking of the prescription drug types by lifetime (table 1) or past year (figure 2) use. Residents in all specialties reported higher rates of unsupervised use of benzodiazepines and amphetamines than of barbiturates and prescription opiates. Rates of amphetamine and prescription opiate use in the past year were low (4.7% or lower for all specialties), and past year use of barbiturates was negligible. Benzodiazepines, however, were clearly the preferred type of prescription drug for all

specialties; 9.4% of all residents had engaged in unsupervised use of benzodiazepines in their lifetime.

Specialties that showed higher rates of unsupervised use of prescription substances included anesthesiology, with the second highest lifetime use of amphetamines (prevalence=29.6%, 95% confidence interval=21-38, $p=0.02$), and pathology, with the highest lifetime use of prescription opiates. Psychiatry had the highest lifetime and past year rates for both benzodiazepine and amphetamine use (benzodiazepines: lifetime prevalence=50.0%, 95% confidence interval=40-60, $p=0.0001$; past year prevalence=27.3%, 95% confidence interval=18-37, $p=0.0001$). Emergency medicine residents were the second most likely to have used benzodiazepines in their lifetime and in the past year, but the rates were nearly half those of psychiatry. Surgeons tended to report lower rates of use for all prescription substances and were among the specialties least likely to have used benzodiazepines in their lifetime (prevalence=16.4%, 95% confidence interval=12-21, $p=0.008$), along with pediatric residents (prevalence=16.4%, 95% confidence interval=11-22, $p=0.008$). Pathology residents tended to have lower rates of use in the past year for all prescription drugs except benzodiazepines.

Are Residents in Some Specialties More Likely to Be Multiple Drug Users?

The mean number of drug types used by respondents in each specialty was calculated for past month, past year, and lifetime use in order to address this question. All 11 substance types were counted, including alcohol and cigarettes. Table 2 presents these results in rank order, beginning with those specialties that reported lifetime use of the fewest number of substances (i.e., family/general practice residents). Little difference was observed in past month and past year means across the specialties except for emergency medicine and psychiatry residents, who tended to use more substances than residents in other specialties.

TABLE 1 (continued)

Opiates ^b		Psychedelics ^c		LSD		Barbiturates	
%	CI ^a	%	CI ^a	%	CI ^a	%	CI ^a
11.2	5-17	19.1	12-26	14.7	8-21	12.1	6-18
10.0	2-18	24.0	12-36	20.4	9-32	4.1	0-9
6.7	4-10	12.2	8-16	11.3	7-15	6.7	4-10
7.5	5-10	14.5	11-18	9.9	7-13	7.8	5-10
11.2	5-17	12.8	7-19	11.0	5-17	10.2	5-16
15.7	6-26	17.6	7-28	11.8	3-21	13.7	4-23
9.0	5-13	17.5	12-23	10.7	6-15	7.3	4-11
14.8	7-22	30.7	21-40 ^c	30.7	21-40 ^c	11.4	5-18
8.4	3-14	13.7	7-21	15.2	8-23	8.4	3-14
5.8	3-9	12.5	9-17	5.7	3-9 ^c	6.6	4-10
7.2	1-13	17.1	8-26	17.1	8-26	18.6	10-28 ^c
8.2	7-10	15.4	14-17	11.8	10-13	8.5	7-10

Are Residents in Some Specialties More Likely to Be Daily Users?

A single episode of use does not indicate a serious pattern of drug use. Daily use, defined as use of a substance 20 or more times in the past month, provided a measure of frequent use. Daily use of any substance was relatively rare for this population. Of the 1,754 respondents, only 85 (5%) were daily users of alcohol, only 65 (4%) smoked half a pack or more of cigarettes each day, only five (0.3%) used marijuana daily, and only one (0.1%) was a daily amphetamine user. There were no daily users of other substances.

Sufficient numbers of daily users for specialty comparisons existed only for alcohol and cigarette use. Psychiatry residents had the highest prevalence (9.1%) of daily cigarette use (half a pack or greater), with 3.7% of all residents reporting daily use. Psychiatry residents also had the second highest prevalence of daily alcohol use (9.1%). Pathology residents had the highest prevalence of daily alcohol use (11.8% compared to a mean of 4.9% for all residents) but were least likely to be daily cigarette smokers. Obstetricians showed a reverse pattern, with the second highest percentage (6.4%) of daily cigarette smokers and the lowest percentage (1.9%) of daily alcohol users.

The five daily marijuana users were distributed among five different specialties. Although no subjects reported daily use of cocaine, one reported cocaine use six to nine times during the past month, and five reported using cocaine three to five times in the past month. These cocaine users were distributed among five specialties. Only four respondents reported benzodiazepine use as often as six to 19 times in the past month, and they were equally divided between family/general practice and psychiatry.

Less than 0.2% reported dependence on any substance in the past year, except cigarettes (2.3%). Of these, psychiatry (5.6%) and obstetrics/gynecology (5.5%) had the highest rates of cigarette dependence.

FIGURE 1. Use of Cigarettes and Illicit Substances in the Past Year by 1,754 Resident Physicians, by Specialty

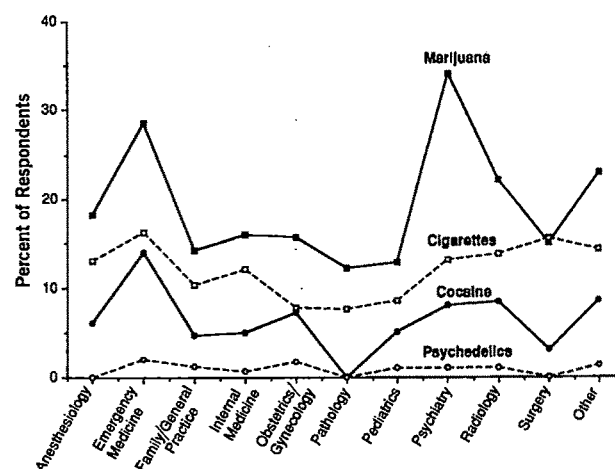
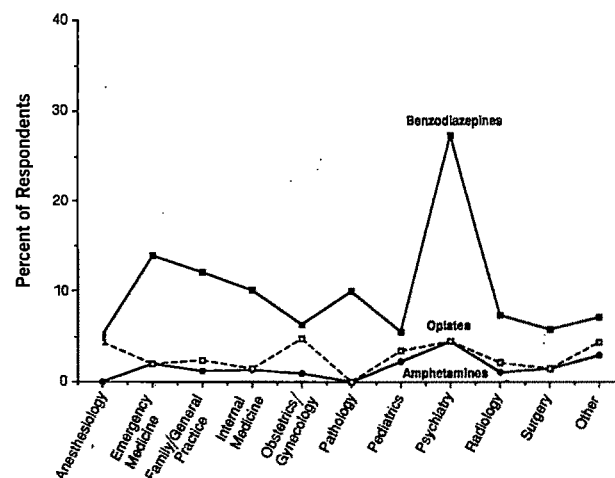


FIGURE 2. Unsupervised Use of Prescription Substances in the Past Year by 1,754 Resident Physicians, by Specialty



These two specialties also had the highest rates of daily cigarette use.

Are Residents in Some Specialties More Likely to Use Controlled Substances Under the Supervision of Another Physician?

Residents were asked if they had taken prescription substances (amphetamines, barbiturates, opiates, or benzodiazepines) under a physician's supervision within the past year. The rates of physician-supervised substance use were very low. None of the respondents reported being prescribed amphetamines in the past year, only 0.6% (N=10) were prescribed barbiturates, 1.3% (N=22) were prescribed opiates, and 1.7% (N=29) were prescribed benzodiazepines. No differences among specialties were observed in the supervised use of any of these controlled substances.

Respondents were also asked if they had used these same four substance types in the past year for self-

TABLE 2. Number of Psychoactive Substances Used by 1,754 Resident Physicians, by Specialty

Specialty	Number of Substances Used					
	Past Month		Past Year		Ever	
	Mean	SD	Mean	SD	Mean	SD
Family/general practice	1.1	0.7	1.4	1.0	2.9	2.1
Pediatrics	1.0	0.6	1.3	0.9	3.0	2.4
Obstetrics/gynecology	1.1	0.7	1.3	0.9	3.1	2.3
Internal medicine	1.1	0.6	1.4	0.9	3.2	2.3
Surgery	1.1	0.6	1.4	0.9	3.2	2.1
Pathology	1.0	0.6	1.3	0.6	3.3	2.5
Undecided/other	1.1	0.7	1.6	1.0	3.6	2.3
Radiology	1.1	0.7	1.5	0.9	3.6	2.2
Anesthesiology	1.1	0.7	1.3	0.9	3.7	2.4
Emergency medicine	1.2	0.9	1.7	1.2	3.9	2.2
Psychiatry	1.4	0.9	1.8	1.1	4.4	2.3

treatment. No specialty use pattern was observed for amphetamines and barbiturates, but residents in family/general practice and psychiatry had a tendency toward self-treatment with benzodiazepines and opiates.

Can the Differences in Observed Substance Use Rates Be Better Explained by Demographic Characteristics Than by Specialty Status Alone?

Specialties did not vary by age but did vary by gender and marital status (table 3). To evaluate whether specialty was associated with drug use independent of demographic characteristics, specialties were stratified by gender and marital status. Past year benzodiazepine and marijuana use was chosen in order to have sufficient numbers of drug users to make meaningful comparisons. Neither gender nor marital status explained differences in use among specialties. For example, both male and female psychiatry residents had the highest rates of benzodiazepine and marijuana use among the specialties. Similarly, marital status had no effect on the rates of benzodiazepine and marijuana use among psychiatry residents.

METHODOLOGICAL ISSUES

This survey has a larger and more representative sample than any previous effort to describe substance use among resident physicians in the United States. However, the limitations in sample size for some specialties in this analysis are recognized. For this reason, 95% confidence intervals are included in table 1. The overall response rate of 60% after three mailings may have been affected by the sensitive nature of the questions, the busy schedules, and high geographical mobility of the subjects. Nevertheless, the response rate compares favorably to that of other drug use surveys of resident physicians (7, 9, 10, 17).

Research on the reliability of substance use surveys suggests that self-reported information on drug use can be reliable when anonymity of subjects is assured (18).

In this study respondents were assured of our inability to link them to their responses. Yet although the anonymous mailed questionnaire generated reliable data on drug use, it did not measure substance abuse and dependence. Prevalence rates represented the percentage of users in the studied population and not diagnosed cases of substance abuse or dependence. Methods for diagnosing substance abuse and dependence are much more expensive and generally require direct interviewer contact and loss of anonymity.

The limited number of specialty choices available to respondents resulted in a group of 72 subjects in the "other/undecided" category. Although findings did reveal some interesting substance use trends among these respondents, their heterogeneity prevented more detailed specialty comparisons. Future questionnaires could be designed to identify respondents in smaller specialties and subspecialties.

DISCUSSION

The resident physicians in this survey were not heavy drug users and did not report dependence on substances other than cigarettes. When compared with a national sample of their U.S. age peers surveyed the same year, they reported lower rates of use for all drugs except alcohol and benzodiazepines (12). We conclude, however, that some specialties were indeed more likely to use specific classes of drugs, to use a greater number of drug classes, and to be daily users of alcohol and/or cigarettes. Specialties did not differ in the legitimate use of controlled substances under the supervision of another physician. Finally, the observed differences in substance use rates were not explained by demographic characteristics.

These findings are consistent with several studies that show psychiatrists at greater risk for substance use than other specialties (1, 2, 8-10). This survey confirms Maddux et al.'s finding that psychiatry residents are more likely to use benzodiazepines (9). Psychiatry residents also reported higher overall rates of marijuana and amphetamine use than residents in other specialties, used more substance types, and were more likely to be daily cigarette smokers and dependent on cigarettes in the past year. Although psychiatry residents were more likely to have tried cocaine, LSD, and other psychedelics in their lifetime, they were not more likely than residents in other specialties to be current users of these substances.

The higher rates of benzodiazepine use by psychiatry residents are of interest, since this class of dependence-producing substances occupies a pivotal position in the specialty's therapeutic armamentarium. Although no data were collected on prescribing practices in this survey, Koch and Knapp (19) reported that psychiatrists were more likely than physicians in 12 other specialties to prescribe controlled drugs. Koch and Knapp did not describe the specific types of substances prescribed by different specialties, but psychiatrists do see patient populations for whom benzodiazepines, and to a lesser

TABLE 3. Demographic Characteristics of 1,754 Surveyed Resident Physicians, by Specialty

Specialty	Number of Respondents	Response Rate (%)	Male ^a		Age (years)		Married ^a	
			N	%	Mean	SD	N	%
Anesthesiology	118	69	87	77	30.9	3.3	79	71
Emergency medicine	50	88	43	86	30.1	2.0	27	55
Family/general practice	260	66	179	70	30.4	2.7	193	75
Internal medicine	467	54	315	69	30.3	3.0	265	58
Obstetrics/gynecology	110	57	63	58	30.0	2.7	67	62
Pathology	52	72	32	63	31.5	4.6	42	81
Pediatrics	179	66	92	52	29.9	2.6	121	69
Psychiatry	89	59	49	56	31.6	4.0	47	53
Radiology	95	72	71	76	30.2	2.7	57	63
Surgery	264	49	219	85	29.5	1.9	170	66
Undecided/other	70	50	44	66	30.7	3.5	48	68

^aPercents were based on the number of respondents for that item.

extent barbiturates and amphetamines, can be legitimately prescribed.

A drug availability or exposure hypothesis might therefore explain higher rates of use for the types of substances prescribed by this specialty, but it would not explain higher rates of use of alcohol, marijuana, and cigarettes. Other possible explanations for higher rates of substance use among psychiatry residents include self-medication for higher levels of perceived anxiety or stress by members of this specialty (20), greater likelihood of prolonged and close exposure to drug-abusing patients, and more extensive training in the use of medications to improve mood and psychological state.

This survey also supports previous studies that identified a higher risk of substance use among emergency medicine practitioners (2, 4, 6). Emergency medicine residents had the highest proportion of cocaine users in the past year and past month and generally higher rates of use of cigarettes, marijuana, benzodiazepines, and psychedelic substances. They resembled psychiatry residents in having more multiple users, but they did not have high rates of daily use. Physicians in this specialty often have significant periods of leisure following long hours of intense, highly stressful duty. They have frequent contact with drug users and have access to most dependence-producing medications in their work. Additional study will be necessary, however, to clarify this specialty-drug use association.

Anesthesiology residents did not report the heavy substance use described in the literature (21). Anesthesiologists were overrepresented among Canadian resident physician drug users (10), impaired physicians treated by Talbott et al. (4), and physicians in the California impaired physicians program (6). Anesthesiologists also have high rates of drug-related deaths (22, 23). Higher rates of use have been attributed to the anesthesiologist's daily handling of dependence-producing substances.

The finding of lower than expected substance use by anesthesiology residents, if substantiated by further data, gives some reason for optimism. It suggests that aggressive preventive efforts in a specialty with previously reported high rates of impairment and identifiable risk factors can lead to a reduction in substance

use. These efforts include preventive education, new procedures to improve accountability for administered narcotics, and formal policies for handling cases of substance abuse (24, 25). Other specialty societies with high rates of substance use might learn from the experience of anesthesiology, but it is not known if risk factors in other specialties, beyond that of drug availability, could be so readily identified and addressed.

Specialties with lower rates of substance use include pathology, pediatrics, and surgery. Pathology residents used fewer types of substances in the past year and past month, were least likely to smoke cigarettes in the past year and month, and were least likely to ever use cocaine. This raises the question of potential preventive influences of residency training in a specialty that dramatically confronts a young physician with the end stages of substance use morbidity. Pathologists are also among the least exposed to one of the hypothesized risk factors in physician drug use—that is, their clinical responsibilities do not require them to prescribe dependence-producing substances.

Pediatricians in this sample were least likely to use alcohol and were among the least likely to use benzodiazepines. Although there is no ready explanation for their lower rates of use, pediatricians tend not to prescribe the types of substances associated with physician impairment. Surgery residents also had consistently lower rates of substance use, especially for LSD, other psychedelics, and benzodiazepines. Their only high drug use ranking was for alcohol use in the past month. The specialties of family/general practice, internal medicine, and obstetrics/gynecology were not among the highest or lowest use groups for most substances.

Despite striking findings on specialty drug use patterns, the data presented in this report do not answer a number of important questions relevant to specialty substance use. For example, are the differences in drug use patterns observed here attributable to the different types of people who enter high- and low-risk specialties or to differences in specialty training and practice environments? What is the influence of variation in drug availability and prescribing practices, specialty-specific stressors, and different levels of supervision and support? Do the substance use patterns of

resident physicians have a direct relationship to more serious forms of drug dependence that appear later in their careers?

Treatment programs and state disciplinary boards have data on sizable samples of impaired physicians that could help clarify some of these issues, but many of these questions can only be resolved in studies with focused questions and samples of adequate size. We are addressing some of these issues in a larger survey of U.S. physician substance use that considers specialty sample size, career stage, and drug availability in the study design.

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Second-Trimester Markers of Fetal Size in Schizophrenia: A Study of Monozygotic Twins

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***Objective:** Since the second prenatal trimester is the critical period of massive neural cell migration to the cortex, and fingertip dermal cells migrate to form ridges during this same period, the authors sought to determine whether there are differences in fingertip ridge count in pairs of monozygotic twins discordant for schizophrenia, possibly indicating that a prenatal anatomical insult affected the twins differently. **Method:** The fingertip dermal ridges of 30 pairs of monozygotic twins (23 pairs in which the twins were discordant for schizophrenia and seven pairs in which both twins were normal) were counted by two persons trained in anthropometric research. Intrapair differences in the counts were then measured, and the differences among the pairs of normal twins were compared with the differences among the pairs discordant for schizophrenia. **Results:** The twins discordant for schizophrenia had significantly greater absolute intrapair differences in total finger ridge count and significantly greater percent intrapair differences than the normal twins; i.e., their fingerprints were significantly less "twin-like." **Conclusions:** The study suggests that various second-trimester prenatal disturbances in the epigenesis of one twin in a pair discordant for schizophrenia may be related to the fact that only one of the twins expresses his or her genetic predisposition toward schizophrenia. This is consistent with a "two-strike" etiology of schizophrenia: a genetic diathesis plus a second-trimester environmental stressor.*

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The task ahead is to discover how genes and environment interact to produce schizophrenia. Of course, it is much easier to talk about such epigenetic interactions than to design experiments that will elucidate them! (1, p. xii)

This twin study was designed to elucidate epigenetic interactions of genes and environment in producing schizophrenia. Genes that predispose to psychosis may be expressed by making individuals

more vulnerable to the disruptive effects of various commonplace prenatal insults. Recent studies indicate that many prenatal insults do not always affect both monozygotic twins to the same extent. We used the monozygotic-twin research strategy to estimate differences in environmental interference that disrupts fetal development in the second prenatal trimester. The second trimester is the critical period of massive neural cell migration to the cortex. Fingertip dermal cells also migrate to form ridges during this trimester. Differences between monozygotic twins in the anatomical dermal feature called "finger ridge count" may serve as "fossil" ("chrono-marker") evidence for any of a variety of factors that might affect one fetus differentially during the second prenatal trimester.

The study of discordant monozygotic twins is one of the most powerful methods used for sorting out the relative roles of genetic and environmental variance in medicine (2-7). For example, recent studies suggest that the monozygotic twin with chronic schizophrenia has larger ventricles and smaller temporal lobes than the nonaffected twin (4). Such important findings in schizophrenia may localize the insult in space, but not in time; that is, the brain cell loss could have occurred at any time prior to the examination.

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Given the lack of confirmation that a single major gene causes schizophrenia (2), there has been renewed interest in studies of monozygotic twins to examine the diathesis-stressor, multifactorial etiology of schizophrenia (2, 3). Unaffected twins in monozygotic twin pairs discordant for schizophrenia (one healthy twin and one schizophrenic twin) are considered to be examples of unexpressed genotypes of schizophrenia, presumably because they did not encounter a putative environmental "stressor" or "releaser" (3). The nature of the stressors or releasers has long been debated (2).

Minor facial physical anomalies (8) and minor physical asymmetries of parallel structures (9–11) are anthropometric markers found in schizophrenia that are known to reflect prenatal insult. However, the pediatric literature associates minor physical anomalies with first-trimester insults. Unlike minor physical anomalies, the embryology and genetics of the anthropometric feature known as total finger ridge count (see Method section for definition) have been thoroughly studied (12, 13). There is no such thing as an "abnormal" ridge count. However, two long-held notions—that fingertip ridge count is one of the most stable and reliable anthropometric measures and that monozygotic twins have nearly identical fingertip ridge counts—have been confirmed in recent studies. These studies show that 1) the ridge counts of monozygotic twins have an intrapair intraclass correlation of 0.96 (14)—in other words, the expected intrapair difference in ridge count between monozygotic twins approaches zero—and 2) tests of interrater reliability in ridge counting for the same individual show a correlation of 0.99 (14). Fingertip ridge counts have correlations of 0.05 and 0.49 in randomly selected individuals and first-degree relatives, respectively (5, 15, 16).

Because healthy monozygotic twins have nearly identical fingerprint ridge counts (5, 14–16), the expected intrapair difference in ridge count between two monozygotic twins free of prenatal injury approaches zero. We used this fact and a study group of monozygotic twins discordant for schizophrenia to try to localize, in time, insults to the fetal brain that may contribute to the expression of schizophrenia-related genes.

Ridge count (unlike more conventional neurodevelopmental markers such as brain ventricle size) is a permanent anatomical feature that is not permanently disrupted by postnatal insults to the subject's brain or body, such as use of psychotropic medication, drug or alcohol abuse, aging, dehydration, or trauma (12, 17–19). For this reason, ridge count remains the mainstay of person-identification techniques (19).

Ridge count has long been replaced by newer methods of determining zygosity, mainly because it is disrupted by various intrauterine insults (12, 13). The only environmental conditions that can change ridge count are intrauterine ones (12, 13, 18, 20–22). Ridge count has therefore been extensively used in recent research on prenatal injury (11, 21–23) and serves as a useful marker of deleterious intrauterine experience (18, 24). Cummins and Midlo (12) were the first to point out

that "dermatoglyphics . . . are significant indicators of conditions existing several months prior to the birth of an individual Dermatoglyphics reflect the existence of differences dating from the fetal period. This freedom from the effects of later environmental influences is shared by few other traits which are accessible to investigation . . . [and] dermatoglyphics may aid in some investigations which call for reconstruction of events in the intrauterine history of an individual" (pp. 185–186).

Recent data, collected with a comprehensive National Institute of Mental Health (NIMH) prenatal history questionnaire for mothers of monozygotic twins, suggest that differences in total finger ridge count between normal monozygotic twins correlate most strongly with second-trimester deleterious events. We administered a questionnaire about deleterious events during pregnancy to a group of 30 mothers of monozygotic twins from a twin registry. We also measured the absolute intrapair differences in fingertip ridge count for each twin pair. The subscale measuring deleterious events that occurred during the second trimester in utero was the best predictor of increased intrapair differences in total finger ridge count and accounted for 36% of the variance. The next best predictor accounted for less than 2% of the variance (unpublished paper of Bracha et al.). A review of the embryological literature also indicated to us that total finger ridge count may be a specific marker for environmental insult in the second trimester of pregnancy (12, 13, 18, 21, 23, 24). Fingertip dermal cells migrate to form ridges (fingerprints) during the second prenatal trimester (13, 18). Abnormalities in fingertip ridge count have been reported in subjects with developmental brain disorders in which second-trimester systemic insults to the fetus are hypothesized to interact with genetic vulnerability (13), including the following: developmental reading disorder (22), some cases of mental retardation (23), fetal alcohol syndrome (25), and in utero viral infections (e.g., rubella and cytomegalovirus) (13, 26–28).

Studies of prenatal rubella infections clearly indicate that although the effect of the virus is paramount, the virus may be necessary *but not sufficient* to produce the clinical entity. Some genotypes cause individuals to be more sensitive than others to the neuropathogenic effects of prenatal rubella (27). Similarly, genes that predispose to schizophrenia may act by merely making individuals more vulnerable to the disruptive effects of various commonplace prenatal insults (3).

There have been several previous ridge count studies of schizophrenia. Most of them were performed before the effects of prenatal insults (e.g., rubella) were discovered and were patterned after studies of trisomy 21 (29). These studies resulted in inconclusive findings (unpublished review paper by Przybyla and Bracha). Three common flaws in the studies were 1) failure to control for genotype, 2) failure to take into account the fact that there is no such thing as an abnormal ridge count, and 3) failure to realize that since ridge count directly correlates with second-trimester fetal size (12,

13, 30), one twin's deviations from the measurements of his or her normal monozygotic twin need not always be in the same direction to be informative. Specifically, in a set of monozygotic twins, one twin's lower ridge count than that of the nonaffected twin is associated with insults which retard the physical growth of the affected fetus during the second trimester (30). Conversely, an affected monozygotic twin's having a higher ridge count than that of his or her nonaffected twin is associated with second-trimester insults that produce generalized fetal edema in the affected twin and thus make the fetal fingertip volar pads larger (13). A discrepancy in ridge count in either direction in monozygotic twins can thus be viewed as a second-trimester fetal size marker (i.e., a chrono-marker) and is the "fossilized" result of random minor, mostly unrecognized insults that caused either growth retardation or edema in the affected twin during that trimester (12, 13).

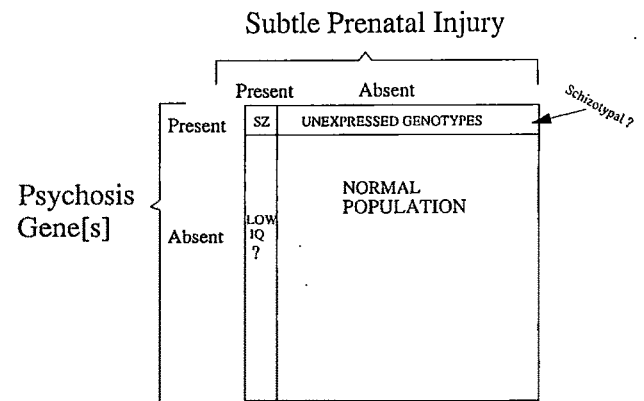
It has recently become clear that many prenatal insults, especially ischemias, frequently do not affect both monozygotic twins to the same extent (18, 31-33). In this study we fully controlled for the genetic contribution to fingertip dermal features by comparing the intrapair differences in fingertip ridge count in two groups of monozygotic twin pairs: twins discordant for schizophrenia and nonpsychotic twins. Slater's well-known sample of monozygotic twins discordant for schizophrenia (5) was far too small to allow this intrapair kind of analysis. We hypothesized that the intrapair differences in ridge count of monozygotic twins discordant for schizophrenia would be larger than those of nonpsychotic monozygotic twins.

METHOD

The study subjects were 23 pairs of twins (46 individuals) from the United States and Canada recruited over a 7-year period (1984-1990) by the Twin Studies Unit at NIMH as part of a large multidimensional study of twins discordant for schizophrenia (4). This group has been exhaustively studied and described in part elsewhere (4, 7). All of the twin pairs were monozygotic, as determined by physical similarities (by I.I.G.) and as confirmed by 19 RBC antigens.

Each individual was interviewed by two senior NIMH research neuropsychiatrists (L.B.B. and E.F.T.) with the complete Structured Clinical Interview for DSM-III-R, Patient Version (SCID-P), parts I and II (34). The SCID videotapes were also examined by a senior clinical psychologist-geneticist (I.G.G.). All psychiatric diagnoses were made according to DSM-III-R criteria. Nine of the 23 pairs were female and 14 were male. Their mean age was 32.5 years (range=19-46) at the time of the analysis. The mean length of discordance was 11.2 years (range=4-24). Discordant pairs with fewer than 4 years of discordance were excluded a priori from the analysis. Belmaker et al. (6) have shown low rates of conversion to concordance beyond the 4-year period. On the basis of risk rates and data from the studies of monozygotic

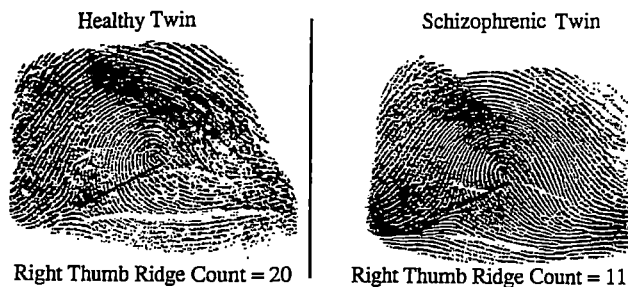
FIGURE 1. The "Two-Strike" Hypothesis of the Etiology of Schizophrenia (SZ)



twins by Pollin and associates at NIMH (6), we estimate that only a few of the 23 discordant pairs are likely to become concordant.

Genes that predispose to schizophrenia may act by making individuals more vulnerable to the brain-disrupting effects of commonplace prenatal insults. Consequently, nonschizophrenic genotypes who suffer a second-trimester insult may manifest ridge count anomalies without manifesting schizophrenia. Therefore, by design, the study group of twins and a comparison group of normal twins should not be matched for prenatal insults or family history (4, 7). Also, by design, the only two requirements for inclusion in the comparison group in this study were no diagnosis of psychotic illness and no known history of prenatal insults according to information from the 39-item NIMH prenatal history questionnaire.

As we have mentioned, the expected intrapair difference in ridge count for monozygotic twins free of prenatal injury approaches zero (5, 14, 15, 35). We obtained the fingerprints of a comparison group of nonschizophrenic subjects consisting of seven pairs of adult monozygotic twins (14 individuals). Three of the seven pairs were male and four were female. Six of the nonschizophrenic pairs had been extensively studied and described elsewhere (4, 7). One subject in each of two of these pairs met the criteria for a single episode of major depression in full remission (DSM-III-R diagnosis 296.26) when administered the SCID. Four of the pairs were found to have no mental illness (DSM-III-R V code 71.09) according to the SCID (nonpatient version). The seventh pair of nonschizophrenic monozygotic twins (72-year-old sisters) was recruited mainly because of its high genetic loading for schizophrenia (one younger sister with chronic schizophrenia and one aunt with an early onset of psychosis). This caused the pair to be especially valuable for the study because, according to the "two-strike" hypothesis of the etiology of schizophrenia (figure 1), normal monozygotic twins who are genetically at risk but do not phenotypically express schizophrenia should not have an elevated intrapair difference in total finger ridge count. This rea-

FIGURE 2. Method Used for Total Finger Ridge Count^a

^aPrints are from one pair of monozygotic twins discordant for schizophrenia.

soning notwithstanding, statistical analyses demonstrated no differences between the pairs of twins discordant for schizophrenia and the normal comparison pairs in the number of prenatal insults as recorded by the NIMH prenatal history questionnaire (unpublished paper of Taylor et al.).

Using standard inking techniques, we obtained prints from each finger on both hands for all subjects (Faurot Crime Detection Equipment, Elmsford, N.Y.). The total finger ridge count analyzed in this article was from the first counting for every subject. Figure 2 shows the method used. All ridges along a straight line connecting the triradial point to the closest point of the core were counted. Ridges containing the point of the core and the triradial point were excluded. The sum of the ridge counts for all 10 fingers yielded the standard total finger ridge count for each person (9, 17, 19). The counting was done by a research assistant (S.K.) who was trained in the standard technique of dermatoglyphic ridge counting (13, 19) and who was unaware of the twins' diagnoses and pair membership.

To establish the reliability of the ridge count data, ridges of all the twins studied were also independently counted by a trained medical geneticist (B.P.). After this second counting, an intraclass correlation coefficient was computed. The resulting correlation for the two raters was 0.98, indicating a high degree of reliability of the ridge count data.

By design, family history was not an exclusion criterion for the normal comparison group, nor was prenatal insult an exclusion criterion for the twins discordant for schizophrenia. Data on twins are unique because an individual can serve as his or her twin's "built-in" comparison subject. In other words, studies of monozygotic twins allow a powerful and unique design in which the unaffected member of each pair can be viewed as the affected member before he or she was affected (3, 4, 7). Our data were accordingly analyzed in two ways.

First, the intrapair difference in total finger ridge count was obtained for each pair, resulting in 23 difference scores for the twins discordant for schizophrenia and seven for the comparison group. Because any discordance in total finger ridge count is important regardless of direction (plus or minus), the absolute value of

the difference was used. A mean of these absolute intrapair differences was obtained for each group. Because of the small size of the comparison group, the unequal group sizes, and the lack of assumption of normality for the data being analyzed, a nonparametric statistic (the Wilcoxon two-sample rank sum test) was computed to test whether the mean differences in total ridge counts for the two groups were significantly different.

Second, we analyzed percent intrapair differences, because in pairs with genetically low total finger ridge counts, even a small absolute discrepancy translates into a relatively high percent difference. For the group of twins discordant for schizophrenia, the unaffected twin's total finger ridge count was used as the denominator, and the resulting value was expressed as a percentage (affected twin's total finger ridge count minus unaffected twin's total finger ridge count, divided by unaffected twin's total finger ridge count, multiplied by 100). For the seven pairs of normal comparison twins, there was no obvious reason to place the total finger ridge count of one of the twins in the denominator, so the smaller total count of the two was used (one twin's total finger ridge count minus the other twin's total finger ridge count, divided by the smaller of the two counts, multiplied by 100). This conservative approach maximized the size of the difference in the comparison group, and this maximization was in the direction of the null hypothesis. Absolute values were also used here. A mean of the percent intrapair differences in total finger ridge count was calculated for each group, and again the nonparametric Wilcoxon two-sample rank sum test was used so as to avoid assumptions about the normality of the distribution.

There was one outlier pair at more than three standard deviations above the mean in the group of twins discordant for schizophrenia, and the Wilcoxon two-sample rank sum statistic was computed for both analyses to test for significant differences with this pair removed. We also tested for any effect of gender by using a Wilcoxon two-sample rank sum test on absolute intrapair differences and percent intrapair differences in both the group of twins discordant for schizophrenia and the normal comparison group, with gender as the grouping factor. Since our hypothesis was clearly in one direction, we used the one-tailed probability value for all analyses, and alpha was set at $p < 0.05$.

RESULTS

Table 1 displays total finger ridge counts, absolute intrapair differences, and percent intrapair differences for the twins discordant for schizophrenia, and table 2 shows the same data for the normal comparison twins. The results of the analyses for mean percent intrapair differences are shown in figure 3.

The mean absolute intrapair difference in total finger ridge count for the group of twins discordant for schizophrenia (12.2, $SD=9.7$) and that for the comparison group (4.4, $SD=5.2$) were significantly different

TABLE 1. Total Finger Ridge Count, Absolute Intrapair Difference, and Percent Intrapair Difference for 23 Monozygotic Twin Pairs Discordant for Schizophrenia

Twin Pair	Sex	Total Finger Ridge Count		Absolute Intrapair Difference	Percent Intrapair Difference
		Schizophrenic Twin ^a	Nonschizophrenic Twin ^b		
1	F	115	96	19	19.8
2	F	163	143	20	14.0
3	F	154	137	17	12.4
4	M	132	122	10	8.2
5	M	141	131	10	7.6
6	M	92	87	5	5.7
7	M	151	143	8	5.6
8	M	196	186	10	5.4
9	F	137	131	6	4.6
10	F	214	206	8	3.9
11	M	135	130	5	3.8
12	F	182	176	6	3.4
13	M	220	215	5	2.3
14	M	149	146	3	2.1
15	F	97	99	-2	-2.0
16	F	192	202	-10	-5.0
17	M	78	84	-6	-7.1
18	M	187	203	-16	-7.9
19	M	154	177	-23	-13.0
20	M	107	129	-22	-17.1
21	M	43	55	-12	-21.8
22	F	29	39	-10	-25.6
23	M	43	90	-47	-52.2

^aMean=135.4, SD=53.6.^bMean=136.0, SD=48.9.

($z=-2.4$, $p=0.008$). This finding was in the hypothesized direction, i.e., a greater difference in the discordant group than in the comparison group.

The mean percent intrapair difference in total finger ridge count for the group of twins discordant for schizophrenia (10.9, SD=11.2) and that for the comparison group (2.8, SD=2.9) were also significantly different ($z=-2.5$, $p=0.006$). This finding was also in the hypothesized direction.

No significant effect of gender was found in either of the two groups. The mean percent intrapair difference in total finger ridge count of the twins discordant for schizophrenia was 10.08 for the female pairs and 11.14 for the male pairs.

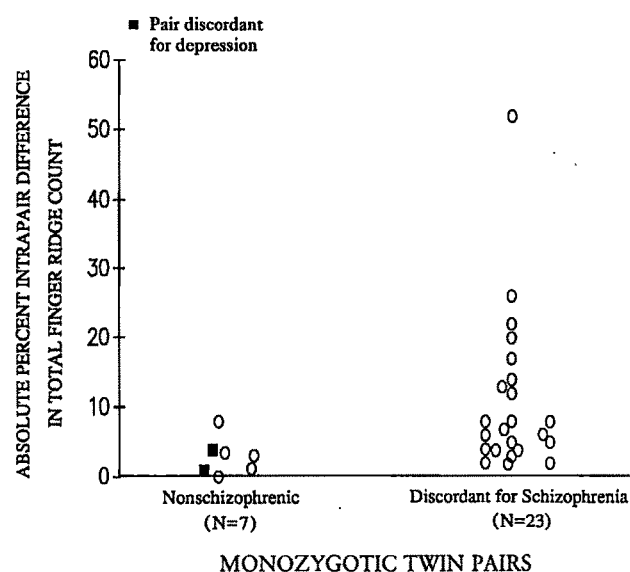
Also, when we recomputed the analyses of mean absolute intrapair differences and mean percent intrapair differences in ridge count between the two groups, with the outlier pair removed from the group discordant for schizophrenia (N=22), the differences between groups remained significant.

DISCUSSION

To our knowledge, this is the first report of a study in monozygotic twins of a quantitative prenatal insult marker in an adult medical condition. The monozygotic twins discordant for schizophrenia had a higher intrapair discrepancy in fingertip ridge count than the nor-

TABLE 2. Total Finger Ridge Count, Absolute Intrapair Difference, and Percent Intrapair Difference for Seven Monozygotic Normal Twin Pairs

Twin Pair	Sex	Total Finger Ridge Count ^a		Absolute Intrapair Difference	Percent Intrapair Difference
		Twin 1	Twin 2		
1	F	125	125	0	0.0
2	M	123	124	1	0.8
3	M	194	196	2	1.0
4	F	113	116	3	2.7
5	F	149	154	5	3.4
6	M	152	158	6	4.0
7	F	179	193	14	7.8

^aMean=150.0, SD=30.4.**FIGURE 3. Percent Intrapair Difference in Total Finger Ridge Count for Monozygotic Normal Twin Pairs and Twin Pairs Discordant for Schizophrenia^a**^a $p=0.006$, Wilcoxon's two-sample rank sum test.

mal twin pairs; i.e., their fingerprints were significantly less "twin-like." This finding extends our previous quantitative clinical study in which we found more minor physical anomalies in the hands of the probands in the same monozygotic twin sample (36).

Ridge count, like height, is under polygenic control (17). Ridge count is increased, for example, in patients with monosomy of the X chromosome (Turner's syndrome), and it is decreased in Klinefelter's syndrome (47,XXY). It is also decreased with the deletion of the short arm of chromosome 5. The effect of these genetic aberrations on ridge count is presently thought to be indirect and mediated through their effect on fetal size in relation to gestational age (30). A postfertilization somatic mutation affecting second-trimester ectodermal cell migration in the affected twin or a split at the blastocyst stage as suggested by Roberts (37) are two conceivable, though unlikely, explanations for the ana-

tomical differences in ridge count and brain structure between monozygotic twins discordant for schizophrenia. Since discordance for schizophrenia in monozygotic twins is about 50%, such an explanation would assume an implausible postfertilization mutation rate of 50%. The results of the present study are more consistent with a diathesis-stressor, two-strike etiology of schizophrenia (2, 3, 10, 38–40), with differences in ridge count being a marker of the intrauterine insults that have provided the second strike. A similar two-hit etiology for some cancers has been proposed by Knudson (40).

This study suggests that the monozygotic twins discordant for schizophrenia were significantly more discordant in size than the healthy monozygotic twins during the second trimester in utero. Second-trimester conditions that could result in a brain injury coupled with a prenatal size discrepancy (and thus a ridge count discrepancy) between monozygotic twins include the following: anemia, anoxia, ischemia, maternal alcohol or drug abuse, maternal toxin exposure, and twin transfusion syndrome. All of these can produce smaller fetal size and therefore a lower total finger ridge count. In contrast, prenatal infections produce generalized fetal edema (including fingertip edema) and thus a higher total finger ridge count (24, 26). Any of these postfertilization prenatal insults, regardless of the direction in which they affect total finger ridge count, could increase the expression of genetic vulnerability to a psychotic disorder by interfering with cell migration from the germinal matrix to the cortex (41).

The literature clearly indicates that the etiology of schizophrenia in twins is not different from the etiology of schizophrenia in singletons (3). Therefore, the findings of this study should be generalizable to all patients with schizophrenia. Obviously, only a monozygotic-twin research strategy can properly control for genotype and therefore allow us to measure differences in this marker of second-trimester environmental interference with intrauterine dermal cell migration. It has been recently suggested, on the basis of epidemiological data, that some patients with the schizophrenic syndrome have been exposed to infection during the second trimester (42). However, there is a growing consensus that neither genetics nor perinatal complications alone are the sole cause of schizophrenia, even in subgroups of schizophrenic persons (38). The results of this study are consistent with the multifactorial diathesis-stressor, two-strike model of the etiology of schizophrenia (2, 3, 10, 38, 39, 41).

We demonstrated fingertip ridge count evidence for second-trimester insult in about one-third of the monozygotic twin pairs who were discordant for schizophrenia. Not all of the discordant twin pairs displayed this anatomical marker of second-trimester insult. This heterogeneity in schizophrenia is not surprising, because the expression of a psychosis-related gene or genes can probably be increased also by postnatal insults or by prenatal insults that would not alter fetal size (and thus ridge count). Nevertheless, ridge count

may be a more sensitive and more specific marker of second-trimester size in monozygotic twins than either minor physical anomalies or even birth weight. A twin whose size was retarded during the second trimester can easily "catch up" to the unaffected twin in birth weight during the third trimester, because 75% of birth weight is gained in the third trimester (18, 31, 43). This twin study provides direct anatomical evidence that phenotypic schizophrenia in genetically exposed individuals may be associated with various (probably heterogeneous) insults that also affect size in relation to gestational age during the second prenatal trimester.

Ridge count may serve as a moderately sensitive but most specific marker of second-trimester fetal size in future studies of monozygotic twins. Fingertip ridge counts should be obtained and analyzed as a dependent variable in all future studies of psychiatric disorders in monozygotic twins. If replicated, this twin study may also have public health implications regarding the importance of second-trimester prenatal care in preventing the expression of severe adult, adolescent, and child behavioral disorders.

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Smooth Pursuit Ocular Motor Dysfunction in Schizophrenia: Evidence for a Major Gene

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and Joanna Katsanis, M.A.

Objective: Evidence suggests that poor eye tracking relates to genetically transmitted vulnerability for schizophrenia. The authors tested competing models for the genetic transmission of poor eye tracking in a search for major gene effects. **Method:** Samples from three studies (conducted in Minneapolis, New York, and Vancouver, B.C.) were pooled. Probands (N=92) were diagnosed as schizophrenic by DSM-III criteria. Of the comparison subjects (N=171), Vancouver patients were an epidemiologic first-episode group; at other sites unselected admitted patients were studied. First-degree relatives (N=146) of 65 probands were also studied. Eye tracking was measured while subjects followed a horizontally moving, sinusoidally driven (0.4 Hz) spot of light on a screen. Performance was quantified by root mean square error. Data analysis was by complex segregation analysis (Bonney's class D regressive models). **Results:** A single major gene is needed to account for poor eye tracking in schizophrenic patients and their relatives. This gene alone can explain about two-thirds of the variance in eye tracking performance. A single gene alone (regardless of dominance) will, however, not account for the data; polygenic factors are also required. **Conclusions:** Results support postulation of a single gene for ocular motor dysfunction, which may be a risk factor for schizophrenia. Eye tracking may be useful as a gene carrier test in genetic studies of schizophrenia.

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Well-conducted family, twin, and adoption studies support the role of genetics in the transmission of schizophrenia (1-3), although risks to relatives vary among studies (2, 4). The literature justifies the conclusion that a single gene alone cannot account for transmission of schizophrenia (5, 6). It is nonetheless possible that a single gene contributes strongly to risk. A chromosome 5 translocation family (7) and an English-Icelandic linkage study (8) suggest a role for a gene on chromosome 5. However, replication attempts have failed (9, 10).

It may be the case that a major gene, in addition to numerous other genes that are individually not very influential, accounts for risk. Gottesman and McGue (11) recently demonstrated that a moderately common allele of relatively modest effect on risk (10% risk for schizo-

phrenia), together with polygenic factors, can account for the data (12). Two, three, or more genes can also be used to account for the empiric risks (13).

One reason it may be hard to find a gene for schizophrenia is low penetrance (probability of manifesting schizophrenia given a susceptible genotype). For example, if a dominant gene accounted for the transmission of schizophrenia, half of parents and siblings would be carriers. Since roughly 6%-10% of these develop schizophrenia in pre-DSM-III studies (2) versus less than 6% under DSM-III (4), risk to carriers would lie in the range of 12%-20%. This would make it hard to decide whether a nonschizophrenic relative was a gene carrier (14). Prospects of finding a major gene could improve if one had a good carrier test. With suitable carrier tests, and given a strong effect of a putative gene on schizophrenia risk, one could sort relatives by risk category.

Perhaps the currently most promising way to detect putative gene carriers for schizophrenia is eye tracking dysfunction (15, 16). This abnormality has a low base rate (4%-5%) in normal subjects and their relatives (17), is temporally stable (18), and is found in a specific subset of schizophrenic patients and their relatives (17, 19). Eye tracking dysfunction also correlates with schizotypal personality features in relatives of schizophrenic patients (20, 21).

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Recent research has demonstrated that measures of eye tracking dysfunction are bimodally distributed in patients with schizophrenia and in their relatives (17, 22). Further, Iacono et al. (23) studied eye movements in Bassett et al.'s (7) trisomy 5 family and showed that the two schizophrenic, partially trisomic members had eye tracking dysfunction while the three nonschizophrenic, nontrisomic members did not. This suggested an association between eye tracking dysfunction and a genetic abnormality conjecturally tied to schizophrenia.

Two published studies of the familial distribution of schizophrenia and smooth pursuit eye movement dysfunction by Matthysse, Holzman, and colleagues (24, 25) used a "Mendelian latent structure analysis" model, which presumes that the only genetic cause common to schizophrenia and eye tracking dysfunction (in schizophrenic patients' families) is a dominant gene. Neither of these studies tested for a major gene effect against models incorporating only polygenic factors, as needs to be done (26). Further, family and twin data show that a single gene cannot account for the transmission of schizophrenia (12, 13, 27). The data of Matthysse, Holzman, and colleagues, as presented, therefore, neither compel nor uniquely favor a single-gene hypothesis (27-29).

The Mendelian latent structure model makes predictions about familial resemblance for schizophrenia and/or eye tracking dysfunction. If a major gene affects risks for schizophrenia and ocular motor dysfunction, it follows that the gene affects the risk for each trait alone. Therefore, one can test the theory of Matthysse, Holzman, and colleagues by looking at ocular motor dysfunction alone.

In this report we improve on previous efforts to identify single-gene influences on schizophrenia in three ways. First, instead of examining diagnosed schizophrenia, we use a presumably simpler trait, ocular motor dysfunction, specifically related to schizophrenia risk. Second, unlike Matthysse, Holzman, and colleagues (24, 25), we use a quantitative indicator of ocular motor dysfunction rather than dichotomous ratings of eye tracking dysfunction. Maclean et al. (30) showed that using quantitative traits improves the power of genetic analyses. Third, we directly test whether single-gene models fit the data by using standard statistical tests.

METHOD

Subjects

Subjects came from three separate studies in Minneapolis (21), New York (22), and Vancouver, B.C. (17). Probands were recruited from consecutive hospital admissions (Minneapolis, New York) or patients with consecutively reported first onsets of psychosis in a community network (hospitals, clinics, private practitioners, and counseling bureaus in Vancouver). All met *DSM-III* criteria for schizophrenia on the basis of struc-

tured interview. Details of subject selection and diagnosis are given in the cited reports.

Lists of first-degree relatives were compiled from patients and informant relatives. Relatives over age 15 years who lived in specified areas around study centers (e.g., 250-mile radius in Minneapolis) were invited to participate. Informed consent was obtained. Relatives were evaluated by structured interview (Diagnostic Interview Schedule [31] in Vancouver; Structured Clinical Interview for *DSM-III* [32] for other sites) for *DSM-III* schizophrenia. At two sites (Minneapolis and New York) relatives were also evaluated for schizophrenia-related personality disorders (with the Schedule for Schizotypal Personalities [33]). Last, subjects' eye movements were studied. The reader should note that our sampling scheme did not select for or against families that had multiple individuals with schizophrenia.

Community comparison subjects were obtained in Minneapolis and Vancouver. Recruitment involved screening family practice clinic visitors (Minneapolis) or by soliciting volunteers from community institutions (Young Men's Christian Association, union halls, family practices, and community colleges in Vancouver). Normal subjects were screened to exclude those with a personal or family history of psychotic disorders. These comparison subjects were used only for preliminary analyses (discussed later), not for genetic analyses.

Assessment of Eye Tracking Dysfunction

Details of stimulus presentation, response recording, and scoring are given elsewhere (17, 20, 21). Procedures were quite similar across sites. Briefly, a 0.4-Hz sinusoidally driven electronic target oscillated horizontally across a display screen. The target simulates the motion of a pendulum, but rather than transcribing an arc, its movement was restricted to one dimension. The stimulus traverse subtended 20° of visual arc. Eye tracking was recorded for 12 cycles of target motion. For two samples (Minneapolis and Vancouver), eye movements were recorded by electro-oculogram (EOG), while the New York study used infrared recording, digitized at 128 samples. These two types of recording yield measures that correlate very highly (18). Nevertheless, to ensure similarity across samples, all ocular motor recordings were filtered with a 30-Hz low-pass Blackman filter, preserving actual eye movements while reducing non-eye movement signals often found in the EOG.

Eye movements were scored by using a method developed by Iacono and Lykken (34). Each cycle of tracking and target motion was centered and normalized to eliminate amplitude differences between recordings of eye and target movements. When eye position lags behind the target (as it usually does), a phase difference occurs that can artifactually inflate eye tracking dysfunction scores. Therefore, target and eye channels were aligned so as to produce maximal cross-correlation between eye and target channels, minimizing this artifact. The squared difference between target and eye

position was then computed for each digitized sample, and for each cycle the square root of the mean of these squared differences was computed. The median of these cycle-by-cycle error measures constitutes the root-mean-square-error measure of eye tracking dysfunction analyzed in this report. Root mean square error thus provides an estimate of the degree to which a subject's eye movements resemble the motion of the target. All scoring was done in a manner that was blind to subject status and diagnosis.

The root-mean-square-error measure is a relatively global one, which indicates how bad eye tracking is without specifying how it is deficient. We chose it nonetheless because previous work has shown that it has desirable properties for behavior genetic analyses. It has high test-retest reliability (18), shows heritability in twins (34), is bimodally distributed in schizophrenic patients and in their relatives (17), and correlates highly with neuro-ophthalmologic measures of eye tracking dysfunction (e.g., oculomotor gain; reference 22).

Statistical Analyses

We compared samples before pooling them, using one-way analysis of variance. We also looked for age effects (by correlation) and sex effects (by *t* test) on eye tracking.

We then corrected for distributional skewness in root mean square error. Skewed variables cause problems because skewing can lead to simulation of major gene action (35). One remedy is to fit a skewness-reducing transformation along with the genetic model, but this often leads to trouble with parameter estimation. Therefore, we instead estimated a standardized Box-Cox power transform (36) to the comparison subjects' data. The Box-Cox method is flexible, allowing for sophisticated transformations. Logarithmic, square root, and other commonly used transformations occur as special cases of the Box-Cox transform. We estimated a Box-Cox transformation that essentially abolished skewness of root mean square error in our comparison group and applied this same transformation to our patients' families. Because almost all comparison subjects should be free of a relatively uncommon schizophrenia-proneness gene, it is unnecessary to consider major gene effects in this sample. Schizophrenic patients' family data were then transformed (using comparison subjects' transformation) before genetic analysis.

We carried out segregation analyses on transformed root mean square error in schizophrenic patients' families. Segregation analysis is a statistical methodology used to determine the mode of inheritance of a trait from family data. This procedure provides for the evaluation of goodness of fit between an inclusive model and a series of nested models in an effort to refute nested models of interest. Each model yields a likelihood statistic that indicates the probability of observing the data, given that the model is correct. The model fit is evaluated by calculating likelihood ratio χ^2 tests that indicate whether the nested model can be rejected.

That is, if the χ^2 test is significant, the data do not fit the nested model. A nonsignificant χ^2 indicates that the nested model cannot be rejected.

We used the Statistical Analysis for Genetic Epidemiology program REGC (version 3.0) (presented by R.C. Elston et al. at a conference in 1986), which computes Bonney's class D regressive models (37), making three main assumptions. First, there are just three familial influences on eye tracking dysfunction: major genotype, regression on parental eye tracking dysfunction values, and residual sibling resemblance in eye tracking. Second, the gene is a two-allele autosomal locus. Third, within major genotypes, siblings share a common regression on parental values and also share a common correlation with other siblings.

The following is a conceptual outline of the regressive segregation analysis models we used. The models are regression (i.e., prediction) models. They predict offspring genotype from parental genotype according to definite transmission rules, and they predict all the phenotypes (here, eye tracking scores) from the genotypes. These models incorporate both transmission due to major genes (i.e., following Mendel's laws of segregation) and transmission from parent to offspring such as occurs with polygenic inheritance (as when the average height of offspring lies midway between the parents' heights).

The models test the data for consistency with the following predictions, which are derived directly from genetic theory: 1) presence of parent-offspring (vertical) transmission, 2) tendency of eye tracking dysfunction scores to sort into distinct classes of dysfunction (i.e., multimodality or distribution admixture), 3) resemblance between parents and offspring, and among siblings, on eye tracking dysfunction scores that follow Mendelian ratios, and 4) resemblance between siblings over and above that found between parents and offspring. Passing the first test is, of course, required by any genetic model. The second tests whether "segregation" (tendency either to get or not get abnormal eye tracking, without in between cases) is occurring. The third test assesses whether any ostensible segregation is of a kind consistent with genetic, as opposed to, for example, environmental, transmission from parent to offspring. The fourth and final test tells us whether polygenic factors, in addition to a major gene, may be at work.

To capture all these phenomena requires a complex model. The models fit had the following parameters: q (frequency of genetic allele A causing eye tracking dysfunction); μ_{AA} , μ_{AB} , and μ_{BB} (transformed root mean square errors for major genotypes AA, AB, and BB); σ^2 (the within-genotype variance); ρ (this is the result of equating ρ_{PO} , the regression of offspring on parent, and ρ_{SS} , the residual sibling correlation—see later discussion); and τ_{AA} , τ_{AB} , and τ_{BB} (probability of transmitting an "allele" A for major genotypes). We assumed random mating with respect to eye tracking dysfunction, Hardy-Weinberg genotype proportions, no sex effect on root mean square error, and that mother-off-

TABLE 1. Characteristics of Schizophrenic Patients, First-Degree Relatives, and Normal Comparison Subjects in a Study of Genetics of Ocular Motor Dysfunction

Group	N	Number of Women	Age (years)		Root Mean Square Error	
			Mean	SD	Mean	SD
Probands	92	26	25.6	7.3	189.0	144.9
Relatives	146	80	42.4	15.3	176.6	151.9
Comparison subjects	171	91	33.6	14.6	141.4	107.7

spring, father-offspring, and sibling-sibling correlations were all equal. These assumptions appeared justified by our data (see later discussion). In contrast to other computer programs for segregation analysis, to test for no polygenic contribution to a trait, one fits a model that constrains correlations between biological relatives all to be zero.

Parameters were estimated by maximum likelihood, using direct search of the likelihood surface (starting from various initial parameter values), followed by Newton-Raphson iterations. Differences in log-likelihoods for various models yielded likelihood ratio χ^2 tests of model adequacy (see later discussion).

Since families were sampled by virtue of having a schizophrenic proband, an ascertainment correction needs to be made. We adopted a suggestion made by Elston (personal communication), namely, that one correct for ascertainment by conditioning on the proband's exact root mean square error score.

RESULTS

Subject Participation and Description

We recruited 92 schizophrenic patients; no family contained two probands. There were 146 participating first-degree relatives of 65 of these probands. We also studied 137 normal comparison subjects and 34 of their relatives. Sixty percent of all eligible relatives (i.e., over age 15 and living within specified geographical radii of our study centers) were studied in the laboratory. Table 1 shows descriptive statistics for subjects. Table 2 breaks down the numbers of families according to how many and what kind of relatives were tested. A large number of schizophrenic patients (N=27) had no evaluated relatives. These subjects were retained in data analyses because they help estimate the rate of eye tracking dysfunction in probands. This in turn improves our estimated frequency of the genetic allele influencing eye tracking dysfunction.

Among relatives, there were five schizophrenic patients (Weinberg short method morbid risk=4.3%, risk period=15-45 years) in five different families. Eye tracking data were available for four of these. For the two samples in which schizotypal personality was evaluated, 11.8% of relatives qualified for a definite *DSM-III* diagnosis. These values are close to those ob-

TABLE 2. Number of Families in a Study of Genetics of Ocular Motor Dysfunction, by Number of Relatives Evaluated

Number of Siblings Evaluated	0 Parents Evaluated	1 Parent Evaluated	2 Parents Evaluated
0	28 ^a	14	9
1	7	14	3
2	3	4	4
3	0	0	2
4	1	0	2
7	0	0	1

^aIncludes one family in which both the proband and an offspring were evaluated.

served by Baron et al. in a similar family study (38). Since analyses with and without the schizophrenic relatives yield similar conclusions, we kept schizophrenic relatives in the sample.

Preliminary Analyses

Our three samples of probands did not differ significantly on root mean square error ($F=0.94$, $df=2$, 86, $p<0.40$). However, relatives did differ ($F=14.23$, $df=3$, 142, $p<0.001$). This difference was entirely due to the Minneapolis sample relatives' lower root mean square errors. Three considerations led us, nevertheless, to pool all samples for this report. First, bimodality (confirmed by skewness-correcting admixture analysis) was found in both pooled New York-Minneapolis and Vancouver samples (17, 22). Second, results of genetic analyses were similar when all three samples were used or the Minneapolis sample was excluded. Third, the same significance test results for model adequacy occur from including or excluding the Minneapolis sample. Therefore, sample heterogeneity does not account for our findings. We would have tested genetic models for the Minneapolis sample alone to check this further, but the sample was too small.

There were no significant sex differences on root mean square error for members of schizophrenic patients' families. While the age effect was significant, it accounted for just 4% of the variance. Analyses of age- and sex-adjusted data were completely consistent with those from raw data, so only raw data are used here.

Root mean square error was positively skewed (coefficient of excess=2.72). The estimated parameters required to eliminate skewness in comparison subjects were $\lambda_1=-0.24$ (power parameter) and $\lambda_2=-36.50$ (offset parameter). This means that the lower the transformed score, the worse the eye tracking performance.

We looked for evidence of assortative mating. The estimated spousal correlation (after allowing for genetic transmission) was -0.36 ($SD=0.34$, not significantly different from zero ($\chi^2=0.93$, $df=1$, $p<0.40$)). We also tested whether parent-offspring and sibling-sibling correlations differed. If they did, then we would need to fit these correlations separately. They were estimated as 0.29 and 0.32, respectively, not significantly different ($\chi^2=0.16$, $df=1$, $p<0.70$). Therefore, in further analyses

TABLE 3. Segregation Models for Eye Tracking Dysfunction in the Families of 92 Schizophrenic Patients

Model	q ^a	Maximum Likelihood Parameter Estimates				$\tau_{AA}/\tau_{AB}/\tau_{BB}$ ^d	rho ^e	-2 Log Likelihood	χ^2 ^f	df ^g	p
		μ_{AA} ^b	μ_{AB} ^b	μ_{BB} ^b	σ^2 ^c						
Selecting the appropriate null hypothesis model											
Free taus	0.249	-153.9	554.3	627.0	7,620.5	1/0.38/0.02	0.31	856.3			
Mixed	0.249	-154.0	558.6	632.1	7,571.2	1/0.5/0 ^h	0.30	856.9	0.67	2 ⁱ	0.88
Testing for parent-offspring transmission: environmental model	0.955	-190.0	490.6	655.9	6,761.7	0.1 ^h	0 ^h	878.1	21.80	3	0.001
Testing competing genetic models											
Generalized single major locus	0.231	-189.0	530.0	671.9	6,150.8	1/0.5/0 ^h	0 ^h	865.8	8.89	1	0.001
Dominant single major locus	0.031	57.3	57.3 ^h	633.1	10,961.4	1/0.5/0 ^h	0 ^h	887.8	30.91	2	0.001
Residual genetic	1.000 ^h		560.5		23,019.2	1/0.5/0 ^h	0.46	898.3	41.34	2	0.001

^aq=Frequency of genetic allele A causing eye tracking dysfunction.

^b μ_{AA} , μ_{AB} , μ_{BB} =Transformed root mean square errors for major genotypes. High scores indicate good eye tracking.

^c σ^2 =Within-genotype variance.

^d τ_{AA} , τ_{AB} , τ_{BB} =Probabilities of transmitting an "allele" A for major genotypes.

^erho=correlation due to nonmajor gene (polygenic-like) effect.

^fA significant value means that a model can be rejected. Values for all but the environmental model are for a test of the specified model against the mixed model. The environmental model was evaluated against the free taus model (see text for explanation).

^gEqual to the number of constrained parameters in the tested model; parameters are not constrained in the comparison model.

^hParameter was constrained (for residual model, all μ s set equal; for the environmental model, all τ s set equal).

ⁱdf=2 because τ_{AA} in the free taus model was constrained to the boundary value 1 during maximum likelihood iterations.

we assumed that assortative mating was absent and that there was only one distinct correlation rho to be estimated, to which parent-offspring and sibling-sibling correlations were equal.

Segregation Analyses

Results appear in table 3. Column heads denote genetic parameters (see earlier discussion). In the three columns headed " $\tau_{AA}/\tau_{AB}/\tau_{BB}$," each row specifies a different model. A significant χ^2 means that a model can be rejected.

Before we can test the genetic hypotheses of interest, we need a null hypothesis model to serve as a yardstick. This model should be one that fits the data parsimoniously. It must include parameters corresponding to all the genetic models that we wish to test. If it does not, differences between log-likelihoods for the models being compared will not generally be distributed as χ^2 and we cannot compute significance levels.

Therefore, the first lines of table 3 compare two candidate null models, the free taus and mixed models. Both models are very general, having a major gene as well as polygenic-like effects. The free taus model differs from the mixed model in that the former allows the "gene" not to act like a real gene. That is, its segregation is not required to be Mendelian. We illustrate this difference with an example: in the mixed model, the offspring of an AB genotype \times AB genotype mating are required by Mendel's laws to have genotypes AA, AB, and BB in proportions $\frac{1}{4}$, $\frac{1}{2}$, and $\frac{1}{4}$ (ignoring sampling variation), which proportions are generated by the assumption that $\tau_{AB}=0.5$. Also in the mixed model, an AA \times AA mating can produce only AA offspring because each parent transmits the allele A to all its offspring (symbolized $\tau_{AA}=1$); similarly, $\tau_{BB}=0$ under the mixed model. By contrast, in the free taus model, the τ s may

lie anywhere between zero and one. Therefore, the comparison between the first two tabled lines tests whether the major "gene" acts like a real gene and follows Mendel's laws.

In fact, the mixed model fits as well as the free taus model. Furthermore, the estimated τ_{AB} (first line) lies within 1 SE (0.38, SE=0.39) of its theoretical value, 0.5. Therefore, the inference that the major gene shows true Mendelian segregation is supported. This implies that the mixed model is the best standard against which to test the nonenvironmental models below it.

The next line, "Environmental," tests for the presence of vertical (parent-offspring) transmission. In this model, there are three potentially distinct grades of eye tracking performance, but parental performance is not required to predict offspring performance. This is concretely modeled by assuming that, no matter what the parental "genotype," the probability of transmitting the tendency to have high root mean square error is the same, i.e., $\tau_{AA}=\tau_{AB}=\tau_{BB}$. (The actual value estimated, 0.1, is immaterial here.) Therefore, rejecting this model amounts to affirming parent-offspring resemblance. Because the environmental model contains free parameters (three τ s) that are constrained in the mixed model, the environmental model has, for technical reasons, to be tested against the free taus model rather than against the mixed model. (Since these two models have nearly equal likelihoods, here this makes little difference.) From the p value, we see that there is clearly significant vertical transmission. Therefore, the data are consistent with genetic transmission as opposed to, for example, sibling "contagion."

The next test specific genetic models of interest. The first two lines in the third part of the table test models in which all transmission occurs by a single gene. Whether one assumes that the allele A is dominant ("Dominant") or that heterozygotes can lie anywhere

with respect to homozygotes ("Generalized single major locus" model), single-gene models are rejected. Therefore, the hypothesis of Matthysse, Holzman, and colleagues of strictly dominant major gene action is not supported.

The line labeled "Residual genetic" tests whether non-major-gene (quasi-polygenic) factors alone can account for the data. This model is concretely specified by requiring that the three major genotype groups have the same mean, i.e., by requiring $\mu_{AA}=\mu_{AB}=\mu_{BB}$. Again, the actual estimated value for these μ s, 560.5, is immaterial here. This no-major-gene model is decisively rejected. Therefore, at least one major gene is required to account for the data; the polygenic model advanced by Gottesman et al. (2) for schizophrenia does not fit these eye tracking data. The major gene in the mixed model accounts for 68% of the variance in root mean square error.

In untabled analyses, we also tested variants on the mixed model (second line) to see whether simple Mendelian patterns occurred. Purely dominant, exactly additive, and purely recessive patterns (working in concert with residual genetic influences) do not fit these data ($\chi^2=19.83$, $df=1$, $p<0.001$; $\chi^2=23.83$, $df=1$, $p<0.001$; and $\chi^2=23.83$, $df=1$, $p<0.04$, respectively). However, the favored mixed model, in the second line, is rather close to recessive (μ_{AB} is approximately equal to μ_{BB}).

DISCUSSION

To our knowledge, these data provide the first rigorous evidence for a major gene affecting eye tracking dysfunction. In fact, we believe that this is the first such demonstration for any schizophrenia-related biological trait. (Previously reported linkage of schizophrenia to chromosome 5 markers has not replicated.) Our results imply that schizophrenia itself may be influenced in some families by at least one single major gene (despite the inconsistent linkage data). Eye movement dysfunction may help detect gene carriers, potentially improving prospects for genetic analysis. This gene would presumably affect the risk of schizophrenia, but we decline at present to speculate how this might occur.

Matthysse, Holzman, and colleagues' dominant gene theory for eye tracking dysfunction and schizophrenia does not adequately fit our data in that their model proposes dominant gene action alone, while we find recessive action in addition to polygenic-like transmission. However, our results clearly and strongly support their central tenet, namely, a single major gene that influences eye tracking.

Our data do not prove that a single gene is at work. First, replication is needed. Second, other causes of apparent Mendelian segregation need to be considered. For example, McGuffin and Huckle (39) recently facetiously reported finding "the recessive gene for attending medical school." They "showed" that a major gene accounts for the familial nature of becoming a doctor. This example, while sobering, does not cast serious

doubt on our results. Attending medical school is clearly a function of many influential life events, while eye tracking dysfunction is not subject to social selection or influence as far as we know. It is implausible that nongenetic factors happen to mimic a major gene for eye tracking dysfunction.

The potential role of platykurtosis (flattening of the distribution of eye tracking dysfunction scores) also needs to be considered. Eaves (40) gave examples in which correct/incorrect psychological test item scores are cumulated into a total score. If items are very good at discriminating whether individuals possess more or less than a specific (arbitrary) amount of the underlying ability measured by the test, then grossly platykurtotic scores can be found because the test has a distorted measurement scale. If the tested ability is heritable and if such a variable is subjected to segregation analysis, Mendelian segregation could be simulated. However, this is also not a major threat to our conclusions. Our data show not just platykurtosis but replicated outright bimodality (17, 22). This is hard to account for by deficiencies in scaling of the eye tracking dysfunction measure.

Objections might be raised that we should not have transformed our data before segregation analysis. Deciding whether to transform data can be a difficult problem. As pointed out earlier, analysis of untransformed but skewed scores can lead to false positive findings of major gene action. However, it is also true that transforming data to reduce skewness could lead to false negative results, at least when a very common gene of relatively modest effect is at work. Since the effect of transformation, then, is to lower power to detect a single major gene (without raising the risk of falsely finding a gene), and since our results strongly favor a major gene hypothesis, the problem of whether to transform the data does not vitiate our conclusions.

Our data also do not prove that only one major gene accounts for eye tracking dysfunction. Our models allow for heterogeneity only in having both polygenic and major gene causes of eye tracking dysfunction. We were not able to evaluate models that postulate two- or three-gene action. Study of such possibilities awaits general availability of more sophisticated computer programs.

An eye tracking gene may not account for most of the variance in schizophrenia risk. We have shown elsewhere (22) that eye tracking dysfunction accounts for approximately 25% of the variance in risk for a spectrum diagnosis (schizophrenia in addition to schizotypal personality) in schizophrenic patients' families. Any gene discovered here is probably only one cause of schizophrenia.

The analysis of eye tracking and other biological traits related to familial risk for schizophrenia may serve two useful functions. First, it may help us account for more of the risk for this disorder. Second, it may help break down the complex clinical presentation of schizophrenia into more simply inherited biological abnormalities.

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Effects of Sodium Lactate Infusion on Cisternal Lactate and Carbon Dioxide Levels in Nonhuman Primates

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***Objective:** To further the understanding of lactate-induced panic in patients with panic disorder, the authors examined cisternal lactate and carbon dioxide levels in nonhuman primates after infusions of sodium lactate comparable to those used in studies of human beings. **Method:** CSF and venous blood lactate, pH, PCO₂, PO₂, and bicarbonate were measured in five ketamine-anesthetized nonhuman primates, without mechanical ventilation, before and after they underwent infusions of sodium lactate. In addition, the same measurements were made for three of the five subjects who were given saline infusions. **Results:** Despite the development of the characteristic peripheral biochemical effects of infused sodium lactate—increased lactate and bicarbonate levels and metabolic alkalosis—no increases in central lactate or carbon dioxide levels were observed. Saline infusions produced no biochemical effects on venous and cisternal measures. **Conclusions:** The results of this study are in keeping with previous findings of nonpermeability of the blood-brain barrier to anionic compounds such as lactate. They therefore support theories of lactate panic based on cognitive and/or brainstem miscalculation of peripheral somatic sensations.*

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Patients with panic disorder (1, 2) and patients with histories of panic attacks (3) are susceptible to the panicogenic effects of sodium lactate infusion. Despite the clinical and heuristic importance of the lactate panic model, mechanisms for lactate-induced panic remain unclear.

Hypotheses for lactate-induced panic have focused primarily on peripheral metabolic effects, especially since studies have suggested that lactate, largely ionized at a normal pH, does not freely cross the blood-brain barrier (4–7). Dager et al. (8), however, reported an increase in CSF lactate in baboons after infusion of 1.0 M racemic sodium lactate at 10 ml/kg, suggesting that infusion of sodium lactate may directly affect the CNS in inducing panic. However, examination of the methodology of

Dager et al. (8) raises several issues. First, the animals were mechanically ventilated, thus presenting the possibility of inadvertent hypoventilation and a consequent increase in central lactate levels secondary to hypoxia. Second, the animals were anesthetized with halothane, an agent that can alter blood-brain barrier permeability (9–11). Third, the amount of lactate infused was double that which is generally used in the standard clinical procedure for humans. It is possible that this high concentration may have exceeded a threshold for blood-brain barrier permeability to lactate.

The question therefore remains whether sodium lactate, infused at concentrations that trigger panic in susceptible humans, penetrates the blood-brain barrier. If it does so in significant amounts, theories of lactate-induced panic would have to include (or discard) direct CNS effects.

Another theory for lactate panic has been postulated by Klein et al. (unpublished 1985 paper). They hypothesized that peripherally infused sodium lactate stimulates production of bicarbonate, which is metabolized to carbon dioxide and water. The model is based on the fact that bicarbonate penetrates the blood-brain barrier poorly, whereas carbon dioxide traverses readily (12). These authors suggested that central hypercarbia triggers an abnormally sensitive “suffocation alarm mechanism” in patients with panic disorder, leading to

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TABLE 1. Baseline Venous Blood and CSF Measures in Five Non-human Primates Given Sodium Lactate Infusions^a

Measure	Blood		CSF		Analysis	
	Mean	SD	Mean	SD	t (df=4)	p
Lactate (mmol/liter)	0.82	0.26	1.99	0.26	-7.18	<0.001
pH	7.45	0.01	7.30	0.03	10.36	<0.0003
PO ₂ (mm Hg)	43.72	13.37	83.79	18.38	-3.97	<0.009
PCO ₂ (mm Hg)	46.70	2.24	49.56	2.63	-1.61	0.09
Bicarbonate (mmol/liter)	31.48	0.07	23.65	1.01	20.39	<0.00002

^aThe repeat baseline values for one subject who had two lactate infusions have not been included.

hyperventilation, a fear of suffocation, and a desire to flee. This central hypercarbia is putatively responsible for the panicogenic effects of lactate (13), inhaled carbon dioxide (14), and infused bicarbonate (15). However in a test of this hypothesis in halothane-anesthetized baboons, Dager et al. (8) failed to find an increase in CSF carbon dioxide levels following racemic lactate infusion.

In an effort to resolve some of the critical questions raised by the findings of Dager et al. (8), we examined lactate distribution and metabolism in nonhuman primates by monitoring cisternal measures after saline and sodium lactate infusions. Ketamine anesthesia was used in this study to avoid the need for mechanical ventilation, and a racemic lactate infusion, paralleling the concentration used in human studies, was administered.

METHOD

Five adult male Bonnet macaques (*Macaca radiata*) served as subjects. Their mean weight was 7.72 kg (SD=0.97, range=6.6–9.3), and their mean age was 5.83 years (SD=0.75, range=5–7). All five subjects underwent 0.5 M lactate infusions, and one subject underwent a repeat 0.5 M lactate infusion. Three of the five subjects also underwent saline infusions, and one of these three subjects subsequently received a 1.5 M lactate infusion.

After transfer from their home cage to a squeeze cage, the subjects were rapidly injected with ketamine, 10 mg/kg i.m. Once anesthetized, the animals were transported to a surgical area and observed for a period of 40 minutes before the first blood and CSF sampling. In general, the animals required 50 mg i.m. of ketamine every half-hour to maintain adequate anesthesia. In the case of replicated procedures (saline or lactate), the timing of ketamine injections was matched to that used in the animal's previous procedure. At least 7 days intervened between trials. On the basis of pilot data, the 40-minute delay before sampling was instituted to avoid the possibility that endogenously produced lactate resulting from the capture procedure would obscure assessment of the exogenous infused lactate. Under these conditions, endogenous serum lactate levels return to baseline by 40 minutes after capture.

After 40 minutes, 3 ml of venous blood were drawn for determination of serum lactate levels and blood gas measurement (pH, PCO₂, PO₂, bicarbonate level, and oxygen saturation). In addition, 2 ml of CSF were obtained, by cisternal tap with a 3/4-inch 23-gauge needle, for making the same measurements. Once the fluid samples had been obtained, either racemic sodium lactate (0.5 M, 10 ml/kg) or an equal volume of 0.9% saline solution was infused intravenously at a constant rate for a total of 20 minutes. (To assess the possibility that membrane permeability might be enhanced at a considerably higher concentration, an infusion of 1.5 M lactate, 10 ml/kg, was administered to one of the subjects who had been tested at the lower level.) Immediately following the infusion, samples were again obtained for making the same measurements that had been made before infusion. (Similarly, to determine whether ketamine anesthesia might reduce permeability to the lactate, one subject was tested according to a different procedure. This subject was manually restrained and infused with 0.5 M lactate before ketamine administration. After the 20-minute infusion, this subject was anesthetized with ketamine as described, and a CSF sample was drawn.) Fluids for gas measurements were collected in heparinized syringes, immediately stored on ice, and assayed shortly afterward. Samples for lactate measurements were collected in tubes with sodium fluoride anticoagulant and assayed immediately.

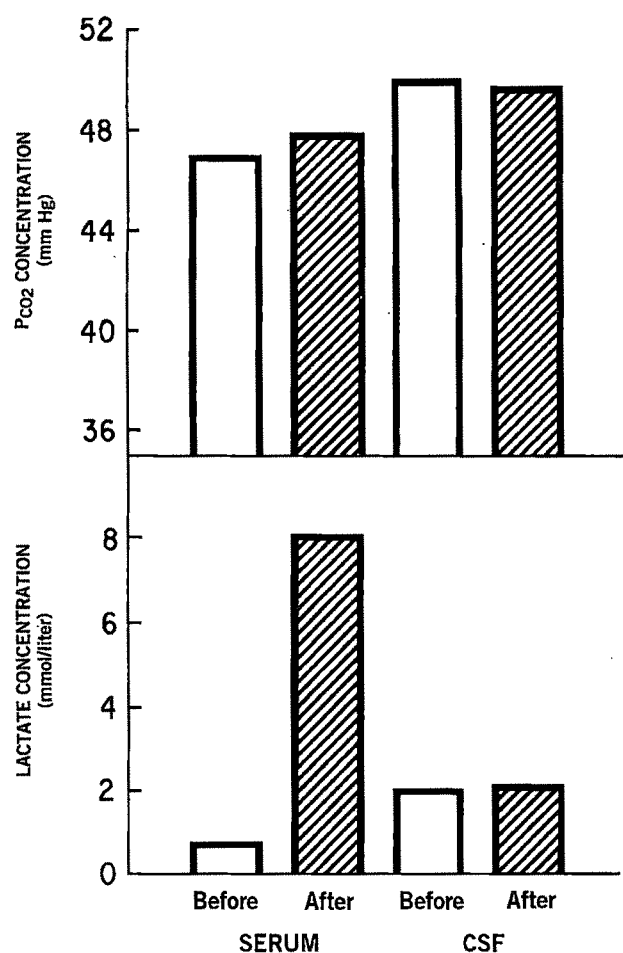
Levels of L-lactate were measured with the Du Pont automatic clinical analyzer (16). This method is a modification of the Marbach and Weil method (17), which uses the oxidation of lactate to pyruvate by rabbit muscle lactic dehydrogenase. Gas measurements were performed on a radiometer ABL3 blood gas analyzer. The precision of measurement for all determinations (pH, PCO₂, PO₂) had a coefficient of variation of less than 2%. Bicarbonate level and hemoglobin oxygen saturation are calculated from these measurements.

We used t tests to compare preinfusion blood and CSF measurements (means were used for repeated procedures) and to compare serum and CSF lactate, PO₂, PCO₂, pH, and bicarbonate levels before and after lactate infusion. Since only three subjects received the saline infusion, conclusions were drawn from the findings of this procedure after inspection only.

RESULTS

At baseline, venous blood lactate levels were significantly lower than CSF lactate levels, whereas blood pH was significantly higher than CSF pH (table 1). PO₂ was consistently higher in CSF than in venous blood, whereas there was a trend for higher PCO₂ in CSF than in venous blood. Bicarbonate levels were consistently lower in CSF than in venous blood. Thus, in accordance with findings in previous studies (18), we found that CSF is relatively acidotic and arterialized and has high lactate levels when compared to venous blood.

As reflected in figure 1 and table 2, serum lactate lev-

FIGURE 1. Effects of Lactate Infusion on Venous and Cisternal Measures in Five Nonhuman Primates

els increased more than tenfold after lactate infusion. (It should be noted that all three subjects who had infusions of saline showed a decrease in lactate levels after infusion: mean=0.97 mmol/liter, SD=0.45, before infusion; mean=0.50 mmol/liter, SD=0.17, after infusion. This suggests that the animals had still not fully reached basal levels of serum lactate even 40 minutes after capture, nor had the ketamine anesthesia stimulated anaerobic metabolism.) In contrast to the enormous rise in serum lactate after lactate infusion, there was no significant increase in CSF lactate levels. Although four of the five subjects showed a minimal increase in CSF lactate levels, it should be noted that two of three subjects also showed similar minimal increases following infusion of saline (overall means were 1.77 mmol/liter, SD=0.15, before infusion and 1.87 mmol/liter, SD=0.12, after infusion).

The subject receiving the 1.5 M concentration of lactate showed an increase in blood lactate from 1.9 mmol/liter to 26.4 mmol/liter (triple the level observed in this subject after the 0.5 M infusion). Nonetheless, the subject's CSF lactate level rose only modestly, from 1.9 to 2.6 mmol/liter (compared to an increase from 1.9 to 2.1 mmol/liter after the 0.5 M infusion). Thus, a

TABLE 2. Venous Blood and CSF Measures in Five Nonhuman Primates Before and After Sodium Lactate Infusion^a

Measure	Before Infusion		After Infusion		Analysis	
	Mean	SD	Mean	SD	t (df=4)	p
Lactate (mmol/liter)						
Blood	0.76	0.18	8.04	2.24	-7.65	<0.0008
CSF	2.02	0.23	2.10	0.26		
pH						
Blood	7.45	0.02	7.53	0.03	-7.32	<0.0009
CSF	7.29	0.03	7.31	0.04		
PCO ₂ (mm HG)						
Blood	46.90	2.28	47.80	2.86		
CSF	49.96	1.84	49.65	2.93		
Bicarbonate (mmol/liter)						
Blood	31.44	0.76	39.88	0.99	-12.51	<0.0002
CSF	23.20	1.03	24.35	1.11		

^aMean values for a subject who had two 0.5 M lactate infusions have been included.

1289% increase in venous serum lactate was associated with only a 36% increase in CSF lactate. Similarly, the restrained subject infused before receiving ketamine showed only a minimal rise in CSF lactate despite blood lactate levels triple those of the anesthetized subjects (undoubtedly because of heightened endogenous lactate production due to muscular activity).

There was a significant increase in blood pH following lactate infusion (table 2), whereas pH dropped modestly in all three subjects after saline infusion (mean=7.44, SD=0.01, before infusion and mean=7.42, SD=0.01, after infusion), probably due to a respiratory-depressant effect of the ketamine. CSF pH levels remained quite stable from before lactate infusion to after infusion (table 2). After 1.5 M infusion, the subject's peripheral pH increased from 7.46 to 7.70, whereas cisternal pH remained relatively constant (7.32 to 7.35).

Blood measurements of PCO₂ before and after lactate infusion did not differ significantly (figure 1 and table 2), nor were there any effects of the saline infusions (mean=46.90 mm hg, SD=1.30, before infusion and mean=48.40 mm hg, SD=2.70, after infusion). Similarly, CSF PCO₂ values before and after lactate infusion were not significantly different (figure 1 and table 2), nor did they differ after saline infusion (mean=47.80 mm hg, SD=4.40, before infusion and mean=51.80 mm hg, SD=1.60, after infusion). Following 1.5 M lactate infusion, the subject's central PCO₂ also remained relatively unchanged (45.50 mm hg to 44.90 mm hg).

Serum bicarbonate levels increased following lactate infusion (table 2) but were relatively unchanged following saline infusion (mean=31.73 mmol/liter, SD=0.15, before infusion and mean=29.43 mmol/liter, SD=4.01, after infusion). In spite of the significant increases in serum bicarbonate after lactate infusion, CSF bicarbonate levels increased only modestly following lactate infusion (table 2); following saline, the mean level increased from 24.37 mmol/liter (SD=0.15) to 29.43 mmol/liter (SD=4.01). After the 1.5 M infusion, the ani-

mal's peripheral bicarbonate level rose from 32.00 to 45.20 mmol/liter, whereas the central bicarbonate level remained relatively stable (22.90 to 24.30 mmol/liter).

No clear pattern of response was observed in blood or CSF PO_2 measures in either infusion condition.

DISCUSSION

The peripheral measures were generally in accordance with those obtained in clinical lactate infusions (1, 2). Increased blood lactate was accompanied by metabolic alkalosis and an increase in bicarbonate levels. In contrast to clinical lactate infusions, however, there was no consistent evidence for hyperventilation on venous PCO_2 , PO_2 , or oxygen saturation measures, although arterial samples are generally required for making an accurate assessment of respiratory function. The absence of increased serum lactate levels and decreased venous pH following the saline infusions suggests that there were no significant respiratory-depressant effects of ketamine.

Despite the induction of the characteristic peripheral effects of lactate infusion, there were no consistent central effects. These negative findings included the absence of cisternal increases in lactate or PCO_2 levels following infusion of lactate. A previous study (8) had reported an increase in cisternal lactate following lactate infusion despite unchanged carbon dioxide levels. Other studies, however, have suggested that the blood-brain barrier is not readily permeable to lactate. For instance, peripherally infused lactate failed to reverse hypoglycemic coma in humans or hypoglycemic seizures in dogs (19), and there are no consistent relations between blood and CSF lactate levels in these two species (18, 20).

Our findings, therefore, are consistent with those of most previous studies but differ from those of Dager et al. (8) with respect to the CSF lactate findings. Several methodological differences may account for this discrepancy. First, Dager et al. infused a 1.0 M concentration of sodium lactate, whereas we used a 0.5 M concentration in the major portion of this study, a level most commonly used with humans. In work with primates, a panic-like pattern, which we term "acute endogenous distress," has been successfully produced with the lower dose (21). Acute endogenous distress is defined as a temporally circumscribed period of motoric agitation and affective distress in the absence of external threat. It is possible that high concentrations of lactate, delivered rapidly, as in our 1.5 M infusion, may be accompanied by modest increases in cisternal lactate, perhaps by exceeding a particular threshold for membrane permeability (8) or as a result of nonspecific osmotic stress (22). The phenomenon, however, does not appear relevant to procedures capable of producing lactate panic in humans.

It should be noted that Dager et al. (8) measured L-lactate and D-lactate combined, whereas only L-lactate was measured in this study. However, Dager et al. (un-

published 1989 paper) indicated that following infusion of high concentrations of racemic lactate, less D-lactate than L-lactate was detected in CSF. Given the absence of an increase in cisternal levels of L-lactate at the 0.5 M concentration, it seems unlikely that D-lactate penetrated the barrier in significant quantities in the current study.

Another source of variation in the findings of various studies concerns the type of anesthetic used. Halothane, used by Dager et al. (8), increases blood-brain barrier permeability to glucose (9) and cocaine (10), although this may only be relevant during conditions of hypocapnia (11). Other studies have used either pentobarbital (20) or, as in this study, ketamine. There is a suggestion (23) that in rats, both agents may reduce blood-brain barrier permeability to a circulating tracer, [^{14}C] α -aminoisobutyric acid. In this study we observed no indication of reduced permeability to lactate due to ketamine.

The absence of a rise in cisternal carbon dioxide in the face of substantially increased systemic lactate and bicarbonate levels is a consistent finding (8, 20). Thus, it appears unlikely that central hypercarbia is a consistent factor in lactate panicogenesis. Most panicogenic agents administered to humans, including racemic lactate (2), D-lactate (24), carbon dioxide (14), sodium bicarbonate (15), isoproterenol (25), caffeine (26), and cholecystokinin (27), produce panic-associated respiratory stimulation. The current and previous studies (8, 20) suggest, however, that peripheral factors may be important for stimulation of the hypothesized hypersensitive suffocation alarm mechanism, but we lack sufficient information at present to substantiate an explanation for lactate panic through peripheral mechanisms.

The data from this study can be seen as supporting a cognitive-behavioral perspective of lactate-induced panic. This model suggests that lactate infusion produces peripheral somatic sensations analogous to naturally occurring panic attacks, which the subject then interprets as an indication of an impending internal catastrophe. Cognitive-behavioral therapy is presumably effective in blocking lactate-induced panic (28) by modifying thoughts of impending catastrophe despite the induction of distressing peripheral somatic sensations.

Alternatively, peripheral cardiovascular stimulation without changes in pH (e.g., with isoproterenol [25]) or activation of chemoreceptors without direct cardiovascular effects (e.g., with carbon dioxide [14]) appears capable of provoking panic. In the case of sodium lactate, both chemical and cardiovascular factors are relevant. In this model, vagally mediated information from the periphery is conveyed to the nucleus tractus solitarius and then to other brainstem structures (13), where it is presumably erroneously evaluated as noxious, triggering both panic and panic-specific respiratory stimulation. These brainstem events may secondarily lead to a cognitive perception of impending catastrophe.

Future studies in nonhuman primates should prove useful in explicating the contribution of both physiological and behavioral-cognitive elements to the elici-

tation of panic. It is essential that we attempt to characterize the neurochemical and pharmacological factors that may be responsible for erroneous information processing at brainstem sites and examine cognitive interventions that may influence interpretation of potentially distressing somatic stimuli.

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Bereavement Reactions Among Homosexual Men Experiencing Multiple Losses in the AIDS Epidemic

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***Objective:** The authors examined whether deaths of lovers and close friends from AIDS increased the frequency of depressive symptoms and depressive disorder in a group of homosexual men. **Method:** Two hundred seven volunteer male homosexual subjects were interviewed in New York City in 1988 and 1989. Depressive symptoms were measured with the Hamilton Rating Scale for Depression, administered by a clinician, and two self-report symptom checklists. Subjects were evaluated for major depression with the Structured Clinical Interview for DSM-III-R. Each subject also reported the number of lovers and close friends who had died of AIDS 1) since the beginning of the epidemic in 1981 and 2) in the 6 months preceding the interview. **Results:** Neither the overall level of depressive symptoms, the presence of specific symptom clusters, nor the presence of a diagnosed depressive disorder was related to the number of AIDS deaths a subject reported in either time frame. In contrast, bereavement reactions specific to loss, namely, preoccupation with and searching for the deceased, were more common in subjects with greater numbers of losses. The findings for depressive symptoms and major depression are not readily explained by measurement artifact, overrepresentation of asymptomatic subjects among study volunteers, habituation effects, numbness, or shallowness of attachments in the subjects. **Conclusions:** Changes in normative expectations regarding AIDS deaths and mobilization against AIDS within the gay community may account for the lack of association between the number of losses resulting from AIDS and the presence of depressive symptoms and depressive disorder.*

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The gay community in the United States has been devastated by the AIDS epidemic. As a consequence, many homosexual men, irrespective of whether they themselves are seropositive for HIV infection, have experienced multiple losses of friends and lovers (1-4). The classic works on bereavement document that loss of a loved one typically produces a range of depressive symptoms. Lindemann (5), Parks (6), Clayton (7), and others (8-12) have described affective, vegetative, and psychophysiological symptoms among bereaved spouses that persisted for at least a year after the death of the partner. An annual incidence rate of 47% for a full depressive syndrome in bereaved spouses has been

reported, representing a sixfold increase over that in a comparable nonbereaved sample (13). Such findings raise concerns that bereaved homosexual men may be at especially high risk for these depressive reactions to loss. Alleviating such responses is an immediate clinical concern. Furthermore, since depression may increase high-risk behavior and reduce compliance with antiviral drug treatments, determining the scope of depressive symptoms and possible moderating factors is of considerable public health importance.

The study reported here examined the effect on homosexual men of multiple losses associated with the AIDS epidemic. In addition to our interest in the clinical and public health aspects of this area, we undertook this investigation as part of a larger effort to expand bereavement research beyond the well-documented areas of spousal, parental, and child death (14, 15).

METHOD

The subjects of this investigation were participants in a study of risk factors for HIV disease progression con-

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ducted in New York City. Recruitment was accomplished through announcements in gay organization newsletters, a newspaper advertisement, and, thereafter, word of mouth (each method secured about one-third of the subjects). Participants were restricted to homosexual or bisexual men aged 18–60 years who had been aware of their HIV serological status for at least 1 month before entering the study. Persons meeting the Centers for Disease Control national surveillance criteria for AIDS (16, 17) were excluded, except for those with esophageal thrush (18).

The baseline examinations, conducted between March 1988 and March 1989, included medical, psychiatric, and psychosocial assessments, supplemented by psychiatric and psychosocial self-rating forms completed approximately 1–2 weeks earlier. Details of the full test battery are presented elsewhere (18–20).

For this study of bereavement reactions, by the term “bereavement” we denote the fact of loss through death of a person to whom one is emotionally attached (21). On the basis of the clinical literature, we decided to examine two conceptually distinct dimensions of psychological response to bereavement: 1) depressive reactions covering a range of affective, somatic, and cognitive complaints that may be sufficiently severe to meet criteria for major depressive disorder and 2) thoughts and feelings specifically focused on the deceased that we denote as preoccupation with and searching for the deceased.

Preoccupation and searching were assessed with the 13-item section on current feelings in the Texas Revised Inventory of Grief (22). This section focuses on the presence of the following subjective experiences at the time of interview: preoccupation with and searching for the deceased (e.g., “I can’t avoid thinking about the person who died”; “Things and people around me still remind me of the person who died”) (four items); tearfulness at the thought of the deceased (e.g., “I still cry when I think of the person who died”) (three items); inability to accept the death (e.g., “I am unable to accept the death of the person who died”) (two items); distress and pain when thinking of the deceased (e.g., “I still get upset when I think about the person who died”; “Even now it’s painful to recall memories of the person who died”) (three items); and anger at the death (“I feel it’s unfair that this person died”) (one item). Items are scored from 1 to 5, with higher scores reflecting more feelings of this type. Item wording was modified only to adjust for the possibility of multiple decedents.

Depressive symptoms were measured with the Hamilton Rating Scale for Depression (23), the depression subscale of the Brief Symptom Inventory (24), and the Demoralization Scale (25); major depression was assessed with the Structured Clinical Interview for DSM-III-R (SCID) (26). The first and last measures were administered in person by a clinician; the middle two are self-report instruments.

The Hamilton scale (17 items) covers the major domains of depressive symptoms in the week preceding interview. Substantial attention is given to somatic

complaints. Scores range from 0 to 53, with scores below 7 indicating lack of clinically significant depressive symptoms. Administration of the scale in this study was aided by the use of a structured interview guide (27) to improve reliability.

The Brief Symptom Inventory is a 53-item rating scale derived from the SCL-90. Its seven-item depression subscale covers dysphoric mood, loss of interest in usual activities, and other nonvegetative symptoms in the preceding week. Scores, expressed as the average item score, range from 0 to 4, with higher scores signifying a greater number of symptoms. Mean scores of approximately 1.8 have been reported for depressed psychiatric outpatients (24).

The Demoralization Scale is a 27-item measure of psychological distress designed for use in the general population. It includes highly intercorrelated symptoms of depressed affect, feelings of low self-esteem, psychophysiological disturbance, and anxiety. Scores can range from 0 to 108; the time frame adopted for this study was the 6 months preceding interview. The mean score in a New York City community sample was approximately 28 (28). Since scores on this scale correlate highly with self-report measures of depressive symptoms (29), in this article scores on this scale are treated as reflecting numbers of depressive symptoms.

The SCID was used to assess the presence of a current episode of major depression. This instrument is a general clinical interview guide that enables clinicians to secure information appropriate for arriving at a diagnosis according to *DSM-III-R*. All interviewers were clinicians with degrees at the master’s level or above who had had extensive previous clinical experience. Interviewer training has been described in detail elsewhere (19). In general, the interviewers were not blind to the subjects’ bereavement status.

In the interview, in response to a modified version of questions developed by Martín (30), each subject enumerated lovers, former lovers, and close friends who had died of AIDS. Each question was asked with reference to the entire period since the start of the epidemic in 1981 and to the 6 months preceding the interview.

The association of number of losses with preoccupation and searching and with depressive symptoms was examined in one-way analyses of variance (ANOVA) using the two-tailed test for linearity with 1 degree of freedom. The association of number of losses with current major depression was tested by using maximum likelihood logistic regression. Losses since the onset of the epidemic were examined first, then losses just in the 6 months preceding interview. (Since preoccupation and searching are specific to persons with loss, the relative rarity of persons with more than one loss in the 6 months preceding interview precluded an analysis of this measure for this shorter time period.) In analyses covering the entire epidemic, numbers of losses were grouped into zero, one, two, and three or more to permit direct comparison with prior research (30). For the 6 months preceding interview, numbers of losses were grouped as zero and one or more. Associations involv-

TABLE 1. Loss of Relationships as a Result of Deaths From AIDS Reported by 207 Male Homosexual Study Subjects

Time Frame/ Relationship Lost	Subjects Reporting No Loss		Subjects Reporting One Loss		Subjects Reporting Two Losses		Subjects Reporting Three or More Losses	
	N	%	N	%	N	%	N	%
Entire epidemic (since 1981) ^a								
Current lover	198	95.6	8	3.9	1	0.5		
Former lover	168	81.6	28	13.6	7	3.4	3	1.5
Close friend	117	56.8	35	17.0	26	12.6	28	13.6
Total ^b	100	48.8	45	22.0	23	11.2	37	18.0
6 months preceding interview ^c								
Current lover	199	97.5	5	2.5				
Former lover	193	94.6	10	4.9	1	0.5		
Close friend	174	84.9	26	12.7	5	2.4		
Total ^b	161	79.3	34	16.7	5	2.5	3	1.5

^aData on some categories of loss are missing for two subjects.

^bThe number of individuals listed in the total in each column does not equal the sum of the numbers in that column because subjects are often enumerated in more than one category of reported loss in a given column.

^cData on some categories of loss are missing for four subjects. These losses are included in the numbers reported for the entire epidemic.

ing continuous variables as the outcome measure of interest—namely, preoccupation and searching, Hamilton depression score, Brief Symptom Inventory depression score, and Demoralization Scale score—were further evaluated using least squares hierarchical multiple regression to afford control of potentially confounding variables, i.e., factors that might be correlated both with losses and with the outcome measure. Such factors—namely, age, HIV status, early signs or symptoms of HIV infection (7), and instrumental and emotional supports—were entered as covariates (in that order) in the regression equation, followed by number of AIDS losses. The measure of social support, derived from Wortman's Social Support Scale (31), assessed levels of emotional and instrumental support available to study subjects in the past month. Associations using major depression, a dichotomous variable, as the outcome were examined again by means of logistic regression, introducing the same covariates as in the least squares regression analyses. Screening of the data for other confounding variables disclosed no additional factors requiring adjustment. In all analyses, statistical significance was established as $p < 0.05$.

RESULTS

The study group consisted of 207 men, 84 HIV negative and 123 HIV positive. In the latter group, 48 men were asymptomatic, 28 were mildly symptomatic, and 47 had significant medical symptoms but not AIDS. The mean age was 38.1 years ($SD=8.5$); 87% ($N=179$) were white, 7% ($N=15$) were Hispanic, and the remainder were black or Asian. The mean number of years of education was 16.4 ($SD=2.7$).

Half of the group reported one or more losses since the start of the epidemic (table 1). Over 20% had experienced a loss in the 6 months preceding interview. These proportions were similar for HIV-positive and HIV-negative subjects.

Preoccupation and searching rose with increasing numbers of losses (of lovers, former lovers, and close friends combined) since the start of the epidemic (table 2). These results were sustained in multiple regression analyses and did not vary by HIV status.

By contrast, the subjects' levels of depressive symptoms did not increase with greater numbers of losses since the start of the epidemic. This result held separately for the Hamilton depression scale, the Brief Symptom Inventory depression subscale, and the Demoralization Scale (table 2) and was unchanged in multiple regression analyses. The possibility of a curvilinear relationship, whereby, for example, Hamilton depression scores rise significantly with the first loss and then decline thereafter, was tested in the multiple regression setting and rejected. The lack of association between loss and depressive symptoms held for the HIV-positive and the HIV-negative men separately.

Similar results were obtained in the analyses of major depression. The overall rate of 3.4% did not vary significantly by number of losses for all subjects combined (table 2) or when subjects were stratified by HIV status. Results from logistic regression analyses adjusted for potential confounding variables produced much the same findings.

Men with and without losses in the 6 months preceding interview did not differ on levels of depressive symptoms or major depression. For example, the mean Hamilton depression score of men bereaved in the preceding 6 months was 3.4, and that of men without recent losses was 4.0. Of the recently bereaved men, 2.4% met criteria for current major depression, compared with 3.6% of those who had not experienced recent losses.

Each of these results for depressive symptoms and depressive disorder persisted in analyses performed separately for loss of lovers, loss of former lovers, and loss of close friends and for subgroups of items on the symptom inventories pertaining separately to depressed affect, somatic complaints, and low self-esteem.

TABLE 2. Preoccupation and Searching, Depressive Symptoms, and Major Depression in 207 Male Homosexual Subjects by Number of Lost Relationships Since the Start of the AIDS Epidemic in 1981

Measure	Total Group of Subjects		Subjects Reporting No Loss		Subjects Reporting One Loss		Subjects Reporting Two Losses		Subjects Reporting Three or More Losses	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Score on preoccupation and searching ^a	32.4	10.6			30.2	11.3	32.2	8.6	35.2	10.5
Hamilton depression score ^b	3.9	3.9	3.8	4.2	4.7	3.8	3.3	3.1	3.3	3.8
Brief Symptom Inventory depression score ^b	0.9	0.8	1.0	0.8	0.8	0.7	0.7	0.9	0.8	0.8
Demoralization Scale score ^b	32.9	17.5	34.3	16.8	32.4	18.3	33.3	21.3	29.4	16.1
Percentage of subjects with current major depression ^c	3.4	1.3	3.0	1.7	4.4	3.1	0.0	0.0	5.4	3.7

^aScores start at the level of one AIDS loss rather than none, since this scale measures reactions specific to bereavement. ANOVA test for linearity, $F=4.45$, $df=1, 101$, $p<0.04$.

^bANOVA test for linearity showed no significant difference.

^cMaximum likelihood logistic regression coefficient was not significant.

DISCUSSION

Among our study subjects, men with greater numbers of losses reported more subjective experiences characteristic of preoccupation with and searching for the deceased than did men with fewer losses. While these findings agree with common sense, previous studies that have described forms of searching for and preoccupation with the deceased have examined reactions to single losses only—most commonly, death of a spouse. As a result, direct comparison of our results with those from other studies is not possible.

In contrast, neither level of depressive symptoms nor rate of diagnosed depressive disorder was related to number of losses, irrespective of type of loss (lover, former lover, close friend) or recency. Even the mean Hamilton depression score for men who had experienced three or more losses was well below the threshold of clinical significance. This result seems counterintuitive and contradicts previous findings in research on bereavement, at least with regard to reactions to a single loss (5–12). While the absence of any discernible effect of losses on depressive disorder may be attributable to limited statistical power, these findings are entirely consistent with the findings for depressive symptoms, and these latter results cannot be as readily discounted. In the following discussion we consider possible mechanisms that would render our results spurious.

Our findings do not arise from psychometric insufficiencies in our symptom measures; the reliability of all three measures is well established (23–25, 32, 33). In our study group, the internal consistency reliabilities of the Brief Symptom Inventory depression subscale and the Demoralization Scale were 0.90 and 0.94, respectively. (Assessment of reliability of the Hamilton depression scale, usually accomplished through interrater studies, was not undertaken.) The Hamilton scale is the most widely used measure of depressive symptoms in clinical research. The Brief Symptom Inventory is used extensively with psychiatric, general medical, and cancer patients (34). Evidence of these two instruments' concurrent and construct validity is substantial. Fur-

thermore, the concordance in our results across the three different scales, as well as with the results of the SCID, excludes artifacts of setting, method of administration, scale length, specific time period and duration of time targeted by the scales, and scope of symptoms as plausible explanations for these findings. While interviewers were often not blind to the subjects' number of losses, we would expect that, if any clinical bias existed, it would be in the direction of overascertainment of depressive symptoms in bereaved individuals.

The men in our all-volunteer study group may not be representative of homosexual men generally in New York City. The problem of generalizability of results pervades much research on homosexual men. It stems from the fact that no sampling frame exists for this population; hence, no random sample can be drawn. It is reasonable to suppose that volunteers are, in general, less depressed and more capable of adaptive responses to loss than other men in similar circumstances. While such selection bias can not be excluded as the source of our results, collateral evidence from another study and alternative logic argue against this explanation.

In 1985 Martin and colleagues (30, 35) initiated a prospective epidemiologic study of the psychological effects of AIDS losses in a group of 745 homosexual men without AIDS in New York City. The group was assembled through diverse methods, including random sampling from members of gay organizations and personal referrals from the initial subjects. Despite this different recruitment method, the group of Martin et al. and our own subjects were nearly identical sociodemographically. Martin and colleagues have conducted yearly interviews with their study subjects, assessing psychological distress in the preceding year with the Demoralization Scale. In 1987 the mean score on the Demoralization Scale was 31.8, no different from that found in our study group. These similarities in sociodemographic characteristics and symptom levels across the two groups suggest that the groups are drawn from the same underlying population rather than that our study subjects represent a specialized, idiosyncratic subgroup.

If AIDS losses are in fact associated with a rise in depressive symptoms in the larger homosexual population, it is worth considering the nature of the selection bias required to produce the results observed in our study. To achieve our null results, less symptomatic men must have systematically volunteered at an increasing rate at each ascending level of loss. At the same time, this process must have acted only on depressive symptoms, not on preoccupation and searching, since these two manifestations did rise with increasing losses. The complexity of such a mechanism, together with our group's apparently typical sociodemographic characteristics and symptoms, renders the argument for selection bias less compelling. Given these considerations, we conclude tentatively that within certain segments of the gay community during the time period of our study, the experience of multiple AIDS deaths did not increase depressive symptoms.

At least four substantive, as contrasted with artifactual, explanations can be advanced for our findings: habituation, denial or numbness, shallowness of attachments, and protective effects of social supports. None of these explanations accords well with the evidence. Habituation should produce a rise in symptoms after one or perhaps two deaths, followed by a leveling off or a decline—not a consistent absence of effects across all levels of loss. Habituation should also blunt emotional responses to loss generally, whereas growing numbers of deaths did trigger increases in subjective experiences characterized by searching. Subjects' open acknowledgment of preoccupation and yearning effectively excludes the argument for denial or numbness. Similarly, these expressions of searching argue against the notion that the relationships severed by death were shallow attachments. Finally, persons with more losses reported significantly more social support, and social support was associated with lower levels of depressive symptoms and depressive disorder. Nonetheless, the absence of any association between depression and loss persisted after adjusting for these mitigating effects of social support.

While we have little direct evidence in this regard, we speculate that two processes operated to minimize the emergence of depressive symptoms. First, the scale of the AIDS epidemic in the late 1980s meant that the untimely death of friends and lovers was gradually becoming an almost "normal" feature of life among homosexual men. Second, the epidemic produced growing social, cultural, and political mobilization within the gay community as a whole (36), as distinct from an individual respondent's mobilization of his own social network. Our subjects were well aware of these activities and were to some degree participants. For example, 80% reported reading gay newspapers regularly, and over 60% were members of gay organizations. These community activities may offer homosexual men some protection against depressive reactions to multiple losses. The comparatively low rate of current major depression overall in this group—3.4%—affords further support for this conjecture. The expected rate of disorder,

adjusted for age and education level, based on the Epidemiological Catchment Area study data for current major depression in males (unpublished data, National Institute of Mental Health, 1988), would be 2.7%. By contrast, Clayton (13) has reported a rate of 16% for a full depressive syndrome among bereaved spouses 13 months after loss.

These findings would help explain certain other results reported by Martin et al. (35). In 1985, 1986, and 1987 the overall Demoralization Scale mean scores were 35.2, 32.9, and 31.8, respectively. Since these men had experienced additional bereavements after 1985, this decline in symptoms is paradoxical if scores increase with growing numbers of losses. Martin et al. also asked subjects about the number of bereavements they had experienced as a result of AIDS. Whereas in 1985 a strong association emerged between increasing numbers of losses and higher levels of demoralization, that association was absent in 1986 and significantly weaker in 1987 than in 1985. These two sets of results (although not interpreted this way by Martin et al.) are broadly consistent with a pattern of decreasing effects of loss on depressive symptoms in the course of the second half-decade of the AIDS epidemic in the gay community.

Our findings require replication in other study subjects before they can be accepted. However, these preliminary results suggest that the gay community has developed effective coping mechanisms to assist members in dealing with multiple losses. On a more theoretical level, our results also suggest that searching and depressive symptoms are by no means necessarily linked components of the bereavement process. Apparently, under certain social and political conditions, the two sets of bereavement reactions may adaptively disengage.

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Need-for-Treatment Criteria for Involuntary Civil Commitment: Impact in Practice

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There has been considerable discussion in the literature on the differences between criteria for involuntary commitment that are based on dangerousness and criteria based on need for treatment. A number of states have adopted clinical criteria, and other state legislatures are actively considering them. Some libertarians argue that dangerousness is constitutionally required if a person is to undergo the loss of liberty involved in commitment. Citing widely publicized data from the state of Washington, they predict that a return to clinical criteria would result in a deluge of inappropriate commitments. Some clinicians counter that use of clinical criteria would result in selection of a much more appropriate clinical population and point to research indicating that strict observation of the need-for-treatment provisions of the APA model commitment statute would actually decrease the number of commitments. The author examines state hospital admission and census data from eight states that added need-for-treatment criteria to their commitment codes between 1975 and 1990 and argues that the data indicate that there is little reason to believe that such changes would result in the deluge of admissions predicted by the critics.

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In the 1970s a series of court decisions, starting with *Lessard v. Schmidt* (1), struck down the existing need-for-treatment criteria for civil commitment as being too broad and too vague. The Hawaii federal district court went so far as to opine that the diagnosis and treatment of mental illness are not acceptable as the basis for commitment because too much is left to subjective choices by individuals who are less than neutral (2).

As a result of such decisions, every state in the country eventually passed statutes making dangerousness to self or to others a requirement for involuntary hospitalization. Many libertarians have concluded that the court decisions indicated that dangerousness was constitutionally required before patients could be deprived of their liberty (3), even though the U.S. Supreme Court has avoided ruling definitively on the issue. In fact, the Court has three times indirectly supported the state's legitimate *parens patriae* interests in providing treatment for those mentally ill who are unable to accept needed treatment because of their illness. In *Jackson v. Indiana* (4), a 1972 case dealing specifically with commitment of persons found incompetent to stand trial, the Court held that "the States have traditionally exer-

cised broad power to commit persons found to be mentally ill The particular fashion in which the power is exercised . . . reflects different combinations of distinct bases for commitment sought to be vindicated. The bases that have been articulated include dangerousness to self, dangerousness to others, and the need for care or treatment or training."

In *O'Connor v. Donaldson* (5), the Court held that "the state cannot constitutionally confine, *without more*, a nondangerous person who is capable of surviving safely in freedom" (emphasis added); the phrase "without more" has generally been interpreted to mean treatment, consistent with the view that provision of effective and needed treatment would be sufficient to justify involuntary hospitalization. Four years later, in *Addington v. Texas* (6), the Court stated, even more directly, that "the state has a legitimate interest under its *parens patriae* powers in providing care to its citizens who are unable because of emotional disorders to care for themselves."

It is true that in its recent decision in *Zinermon v. Burch* (7), the Court, in dicta, cited its previous holding in *O'Connor* but omitted the key phrase "without more," thus again raising questions about its view on commitment for treatment. However, in view of the Court's increasingly clear position in favor of permitting states to set up their own individual procedures to govern admission to their institutions by narrowing the category of legitimate federal constitutional issues, the dicta certainly do not preempt debate on the issue.

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Appelbaum (8), writing before the *Burch* decision, concluded that need-for-treatment criteria were not inherently unconstitutional; rather, the statutes struck down by state and federal district courts had been impermissibly vague and/or overly broad. The situation is similar legally to the Supreme Court's rulings striking down state death penalty statutes in the early 1970s; the Court did *not* rule that capital punishment was unconstitutional but rather that the existing statutes were too vague (9). When more tightly drafted statutes were passed, the Court upheld them (10). A similar process may well occur in the case of civil commitment criteria based on need for treatment.

Over the past decade, following the failure of deinstitutionalization, there has been growing criticism of the dangerousness standard as inadequate to deal with the problems of the chronically mentally ill in the community. Critics have pointed out not only that the criterion of dangerousness selects the wrong types of patients (11) but that restrictive civil commitment criteria (12-14) and economic pressures (15) have led to diversion of mentally disordered persons from the civil to the criminal justice system, where they receive even less care than they did in the civil hospitals from which they were "decarcerated" (16) and are thus released back to the streets in the same condition in which they were arrested.

On the basis of a need-for-treatment model first proposed by Stone (17) and subsequently developed by Roth (18), APA accepted as its official policy some guidelines for statutes governing involuntary hospitalization that provided for commitment based on need for treatment under a guardianship model carefully constructed to prevent the abuses of the previous vague statutes struck down in the 1970s (19). Need for treatment is considered necessary, but not sufficient, for hospitalization. The APA model statute permits commitment either according to the usual criteria of danger to self or others or to prevent substantial physical or mental deterioration. There is also a requirement that the patient be incapable of consenting to either hospitalization or treatment.

The proposed statute drew criticism from libertarians (20) and support from some patient advocacy groups (21) and clinicians (22, 23), but the debate continued to be theoretical and ideological rather than empirically based. Opponents of need-for-treatment criteria feared that the clock would be turned back to the days of unfettered clinical decision making, when more than half a million patients were hospitalized involuntarily. To attempt to answer the question of the impact of need-for-treatment criteria, two research groups tried to estimate those effects by asking emergency room clinicians responsible for commitment evaluations according to existing dangerousness criteria to evaluate the same patients simultaneously according to the APA criteria (24-26). They reported that only 36%-56% of patients committable according to the dangerousness criteria would have been committable according to the need-for-treatment criteria, whereas the great majority of patients committable according to the need-for-treat-

ment criteria would also have been committable according to the dangerousness criteria. Such studies cannot, of course, substitute for empirical research into actual changes in admission patterns following changes in commitment criteria.

While no state has adopted the APA criteria in toto, a number of states have changed their statutes to permit commitment in order to prevent other than purely physical deterioration. After a highly publicized double murder by a mentally ill person who had been refused voluntary admission to a state psychiatric facility, the Washington state legislature revised its standard for the gravely disabled to permit commitment of a mentally ill person who "manifests severe deterioration in routine functioning as evidenced by repeated and escalating loss of cognitive or volitional control over his or her actions and is not receiving such care as is essential for his or her health or safety" (27). Following this "horror story" there was nearly a doubling in state hospital admissions over the period of a year, beginning several months *before* the statute went into effect. The increase was attributed by Durham and various colleagues, in a series of articles, chiefly to the broadening of the commitment criteria (28). Their conclusion has been cited again and again when legislatures in other states have considered need-for-treatment criteria, while little has been published concerning even broader criteria in a number of other states.

After the previous need-for-treatment criteria were replaced by dangerousness standards, there were published studies that documented changes in admissions and census at state mental hospitals. With the exception of the Durham articles, there have been no attempts in the psychiatric literature to investigate changes following the reintroduction of need-for-treatment criteria for commitment. This article reports gross data from eight other states.

RESULTS OF CHANGES TO NEED-FOR-TREATMENT CRITERIA

There have in fact been significant changes in commitment statutes in a number of states besides Washington over the past 16 years. Table 1 shows state hospital admissions in these states before and after changes in their statutes. Since different states provided different types of information, total admissions are reported for four states and involuntary admissions for the remaining three.

In 1975 South Carolina passed a statute providing for commitment of patients who need hospital treatment and because of their condition lack sufficient insight or capacity to make responsible decisions with respect to their admission to a hospital (29). While involuntary admissions rose 14% in the year after the changes (table 1), voluntary admissions rose 51% during the same year, indicating that factors other than the new statutory criteria were the major reasons for a rise in admissions.

TABLE 1. State Hospital Admissions After Statutory Changes in Criteria for Involuntary Civil Commitment^a

State	Admissions						
	2 Years Before New Statute (N)	1 Year Before New Statute		1 Year After New Statute		2 Years After New Statute	
		N	% Change	N	% Change	N	% Change
South Carolina ^b	2,920	2,786	-5	3,184	14	3,495	10
North Carolina ^c	12,101	11,425	-6	11,014	-4	8,104	-26
Alaska ^c	1,060	1,146	8	1,138	-0.1	1,056	-7
Hawaii ^c	291	279	-4	327	17	424	30
Kansas ^c	3,990	4,559	14	4,273	-6	4,163	-2
Texas ^b	11,773	12,722	8	12,323	-3	12,753	3
Colorado ^b	1,520	1,607	6	1,426	-11		

^aData were supplied by an official of each state's mental health department.

^bInvoluntary admissions.

^cAll admissions.

North Carolina revised its statutes in 1981 to permit hospitalization of persons who are unable to care for themselves, as sufficiently demonstrated by their engaging in grossly emotional or inappropriate behavior or displaying other signs of severely impaired insight and judgment (30). Following the change, both admissions and average census at the state's four mental hospitals, which receive approximately 80% of involuntary admissions, actually decreased. The data on North Carolina in table 1 demonstrate consistent decreases in admissions following the broadening of the commitment criteria.

In addition to the changes in criteria for involuntary hospitalization, North Carolina broadened its criteria for initial commitment to outpatient treatment. This was done to permit commitment of a person who is capable of surviving in the community but (on the basis of previous history) needs treatment to prevent further disability or deterioration that would predictably result in dangerousness and whose mental status negates his or her ability to make an informed decision to seek or comply with recommended treatment (31). The state provided capitation grants of \$2,000 per patient to community mental health centers to encourage the use of the new provision. Despite the broader criteria and financial incentives, Hiday and Scheid-Cook (32) reported that only 8.3% of initial commitments were to outpatient treatment.

Alaska revised its statutes, effective in 1985, to provide for hospitalization of a person who, as a result of mental illness, will, if not treated, suffer distress that impairs judgment, reason, or behavior, causing a substantial deterioration of the person's ability to function independently (33). There had been a mild (8%) rise in admissions to the state mental hospital the year before the changes, but after the changes, admissions fell consistently (table 1).

Hawaii revised its statutes in 1986 to provide for commitment of persons who are "obviously ill," defined as a "condition in which a person's current behavior and previous history of mental illness, if known, indicate a disabling mental illness, and the person is incapable of understanding that there are serious and

highly probable risks to health and safety involved in refusing treatment" (34). There was a significant rise in both new admissions and readmissions (table 1); however, the new statutory provisions have rarely been used because of constitutional questions.

Kansas also revised its statutes in 1986, to provide for commitment of patients who suffer severe mental disorders to the extent that they need treatment, lack the capacity to make informed decisions concerning treatment, and are likely to cause harm to themselves or others. "Likely to cause harm" means that the person is "likely, in the reasonably foreseeable future, to cause substantial physical injury or abuse to self or others, or substantial damage to another's property, as evidenced by behavior causing, attempting or threatening such injury, abuse or damage; or is substantially unable to provide for all of the person's basic needs, such as food, clothing, shelter, health or safety, causing substantial deterioration of the person's ability to function on the person's own" (35). After a rise in admissions before the changes in the statutes, both admissions and census fell after the changes (table 1).

Texas revised its statutes in 1987 to provide for hospitalization of persons who, as a result of mental illness, will, if not treated, continue to suffer severe and abnormal mental, emotional, or physical distress, will continue to experience deterioration of ability to function independently, and are unable to make rational and informed decisions about whether to submit to treatment (36). There was an 8% rise in involuntary admissions the year before the changes, which subsequently leveled out (table 1). Voluntary admissions did not fall after the new statute went into effect.

Colorado revised its statutes in 1989 to provide for hospitalization of persons who suffer from chronic mental disorders with psychotic features, who have been hospitalized at least twice within the previous 36 months, and who exhibit a deteriorating course (37). There was a rise in admissions the year before the changes, with a fall in the year after the changes (table 1).

Arizona passed a statute in 1990 that provides for commitment of persons who suffer from "permanent or acute disability" (38). The constitutionality of this stat-

ute has been challenged. A state court of appeals ruled in 1991 that the statute is not too broad because it requires the clear and convincing showing of a severe mental disorder that has a substantial probability of causing severe mental, emotional, or physical harm; it is not too vague because no warning is required for those incompetent to make treatment decisions and because courts are required to make factual findings of a mental disorder with a substantial probability of causing serious injury (39). The ruling was not appealed to the state Supreme Court, but another challenge is currently before a different appeals court. The new provision has been rarely used because many continue to fear that the criterion is unconstitutional. In the 12 months before the new law went into effect, there were 441 involuntary civil admissions to the Arizona State Hospital, while in the subsequent 8 1/2 months, there were 423. If it is found that this trend continued for the rest of the 12-month period, it would represent a 35% increase in admissions; however, patients committed under the new provision do not make up a significant percentage of the new admissions (personal communication, Dr. J. Migliaro, Arizona State Hospital).

DISCUSSION

Since need-for-treatment criteria have been proposed by APA, and passed by the states I have listed, as additions to existing dangerousness criteria rather than as replacements, some initial increase in admissions after passage of such legislation would certainly be expected. After all, if no new patients were to be admitted, there would be no purpose for the legislation. Proponents of need-for-treatment criteria argue that since a major goal of the legislation is to permit early intervention and to provide effective treatment *before* patients deteriorate sufficiently to satisfy the dangerousness requirements, many of the patients committed under this standard would be committed eventually under existing criteria, and at that time they would require more lengthy hospitalization because of the increased severity of their condition.

With the exception of Washington State, the dire predictions by critics of need-for-treatment standards have not been borne out in practice since the passage of such legislation, despite the fact that no state has yet incorporated the protections proposed by APA in its model statute. This fact illustrates the multidetermined nature of admissions to psychiatric facilities (40).

Broader statutory criteria for commitment are most frequently enacted in a jurisdiction in response to specific circumstances that appear to call for a lower commitment threshold, such as publicized horror stories involving mental patients. In such situations, it is not uncommon for commitment rates to rise even without statutory changes (41), as in fact happened in the state of Washington, as well as in Alaska, Kansas, Texas, and Colorado in the year before their broadened criteria went into effect. Therefore, any observed increases

in commitments may be due as much to the social pressures leading to statutory changes as to the changes themselves.

North Carolina, Alaska, Kansas, Texas, and Colorado passed need-for-treatment criteria for commitment, and all experienced decreases in admissions. In Hawaii and Arizona, rates of admission to state hospitals rose contemporaneously with passage of broader commitment criteria, although data from those state hospitals indicated that very few commitments were made under the new criteria, again supporting the conclusion that both changes in commitment laws and rises in admissions may be due to the same underlying social pressures, rather than the conclusion that broadening the commitment criteria was responsible for the rises in admissions. The moderate rise in involuntary admissions following statutory changes in South Carolina was far overshadowed by an almost fourfold greater concurrent increase in voluntary admissions, which could not be attributed to statutory changes.

From the data presented here, it appears that opposition to broadening commitment criteria on the grounds that existing psychiatric facilities would be overwhelmed (as has been argued recently in the debate in the Wisconsin legislature) is misplaced. Concern about the use of costly inpatient resources, often at the expense of funding for community treatment programs, is certainly appropriate; but such concern should be raised on the basis of any social pressure for increased protection from the mentally ill, not just when statutory changes are proposed. In fact, the proposals themselves may be the best indication of such social pressure. And long-term effects need to be taken into consideration; if the goals of early intervention are realized, there should ultimately be a lowering of hospital census figures because of shorter stays.

It also appears that no broadening of commitment criteria should be enacted without specific attention to the resources that might be required for providing treatment. This was not done in Washington (even with the evidence of significant increases in admissions before the statute went into effect) and caused severe problems in service delivery at one state psychiatric hospital. In contrast, by proactively providing additional funding to outpatient facilities, North Carolina successfully anticipated potential problems stemming from passage of its broader outpatient commitment criteria.

Changes in admission and census rates are multidetermined (15, 40) and cannot be simplistically attributed to a single cause, such as changes in commitment criteria. Detailed studies are required, using interviews with knowledgeable persons involved in implementing changes and reviews of clinical and commitment documents, as well as before-and-after admissions and census data. In addition, such studies should be correlated with current events (as is routine practice in individual psychiatric interviews), and data from one jurisdiction should not be automatically accepted as applicable to another until differences in existing administrative and fiscal policies are factored in. When such comprehen-

sive projections are available, they should serve to provide decision makers with relevant information upon which to base their decisions concerning proposed statutory changes.

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The Influence of Topography on the Cognitive and Psychopathological Effects of Tardive Dyskinesia

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Objective: The purpose of the study was to investigate the influence of the topography of dyskinesic movements on their effect on cognitive impairment and negative symptoms. **Method:** Eighty-four inpatients who satisfied DSM-III-R criteria for schizophrenia were rated for tardive dyskinesia, akathisia, and drug-induced parkinsonism, as well as negative symptoms, with the Scale for the Assessment of Negative Symptoms and for cognitive state with the Mini-Mental State examination. The subjects were then divided into those without tardive dyskinesia (N=45), those with orofacial dyskinesia (N=19), and those with limb-truncal dyskinesia (N=20). Differences among the groups were assessed with multiple analysis of covariance (MANCOVA), with age, akathisia, and drug-induced parkinsonism ratings as the covariates. Post hoc Spjotvoll and Stoline tests were then undertaken. **Results:** MANCOVA revealed a significant difference among the groups. Post hoc tests showed that the group with limb-truncal dyskinesia had significantly lower scores on the Mini-Mental State Examination and higher scores on the Scale for the Assessment of Negative Symptoms. The group with orofacial dyskinesia was significantly different from the nondyskinetic group only on the total score for the Scale for the Assessment of Negative Symptoms and the attention subscale. There were no significant differences between the dyskinetic groups. **Conclusions:** After correction for the important confounding variables of age, akathisia, and drug-induced parkinsonism scores, those with limb-truncal and, to a lesser degree, orofacial dyskinesia differed significantly from nondyskinetic comparison subjects in ratings of cognitive impairment and negative symptoms.

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Tardive dyskinesia is one of the most serious consequences of exposure to antipsychotic medication, whose importance rests with its potentially irreversible nature. Tardive dyskinesia may affect most areas of the body. Thus, in addition to the classical linguobuccal masticatory movements, there may be choreiform movements of the arms, legs, and trunk. It has been suggested that this limb-truncal dyskinesia can be usefully separated from orofacial tardive dyskinesia and may differ in its pathophysiology, pharmacotherapy, and cognitive sequelae.

There is, however, little agreement in the literature on the differential effects of orofacial and limb-truncal tardive dyskinesia on negative symptoms and cognition.

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Waddington et al. (1) found an association between these variables only with orofacial tardive dyskinesia. Some studies report only orofacial dyskinesia scores (2), while others report dyskinesia scores without reference to the topography of the dyskinesia (3-5). Others have found a relationship between limb-truncal, but not orofacial, tardive dyskinesia and negative symptoms and cognitive impairment (6, 7).

There may be several reasons for these discrepancies. Most of the studies reporting negative results have been conducted on younger patients, in whom the pathophysiology of tardive dyskinesia may differ (8). The prevalence of limb-truncal dyskinesia is higher in younger age groups (9). Studies with a wide age range may thus show an association between orofacial, but not limb-truncal, tardive dyskinesia and cognitive impairment, resulting from the differences in age structure between the dyskinetic subtypes.

Some studies failed to control for the presence of anticholinergic medication, which may have had an adverse effect on cognition. Other movement disorders may be important confounding variables. Thus, both

TABLE 1. Demographic and Clinical Characteristics of Schizophrenic Patients Without and With Dyskinesia

Group	N	Age (years)		Sex		Duration of Medication (years)		Duration of Hospitalization (years)		Age at Onset (years)		Current Neuroleptic Dose (chlorpromazine equivalents)	
		Mean	SD	M	F	Mean	SD	Mean	SD	Mean	SD	Mean	SD
No dyskinesia (comparison group)	45	56.1	12.3	19	26	27.5	10.5	24.5	9.6	27.9	7.2	601	503
Orofacial dyskinesia	19	60.9	7.8	10	9	28.1	8.9	26.9	6.5	29.1	6.7	528	658
Limb-truncal dyskinesia	20	60.1 ^a	5.8	12	8	29.9	7.1	29.2 ^b	5.8	29.8	7.5	485	396

^aF=2.4, df=2, 81, p=0.08.^bF=2.5, df=2, 81, p=0.08.^cF=24.7, df=2, 81, p<0.000001.^dF=7.4, df=2, 81, p=0.001.

drug-induced parkinsonism and akathisia may coexist with tardive dyskinesia and may also be associated with negative symptoms or cognitive impairment (6, 10, 11).

In this study, we sought to investigate the relationship between both orofacial and limb-truncal dyskinesia and the severity of cognitive impairment and negative symptoms. Age, drug-induced parkinsonism, and akathisia served as covariates.

METHOD

All the residents of several long-term wards at a hospital were screened. For inclusion the patients had to satisfy *DSM-III-R* criteria for chronic schizophrenia, have at least 5 years' cumulative exposure to antipsychotic medication, be cooperative, and be able to give verbal informed consent to assessment. A change in medication in the preceding month, muteness, established neurological disease, a history of significant alcohol abuse, and known intellectual impairment led to exclusion. Because of incomplete case records, we were unable to calculate total lifetime exposure to antipsychotic medication. Current antipsychotic medication dose was calculated in chlorpromazine equivalents (12).

Eighty-four patients satisfied the criteria. They were seen on two occasions, usually 1 week apart, by the two investigators. They were subsequently reviewed 3 months to 2 years later. Only 19 subjects were shared with a previous study (6). Tardive dyskinesia was assessed by the Abnormal Involuntary Movement Scale (AIMS) (13). Because dyskinetic movements can be modified by anxiety and voluntarily inhibited, part of the assessment was performed unknown to the patients while they attempted to memorize a picture for 2 minutes. Tardive dyskinesia was recorded as present in those who satisfied the criteria of Schooler and Kane (14). All dyskinetic subjects would have been classified as "persistent tardive dyskinesia, concurrent neuroleptics" by these criteria.

Akathisia was rated on a scale developed for this purpose (15). Because few subjects had subjective symptoms of restlessness, evidence of particular patterns of objective restlessness, which have been described as be-

ing most discriminating for akathisia, was required. These included an inability to sit still, rocking from foot to foot for more than half the time while standing, fidgety leg movements while lying or sitting, and an inability to stand without walking or pacing (16). Parkinsonism was assessed on the 10-item scale of Simpson and Angus (17). The patients were rated on the Scale for the Assessment of Negative Symptoms (18), the Hamilton Rating Scale for Depression (19), and the Mini-Mental State examination (20).

The subjects were then divided into three groups: those without tardive dyskinesia, those with orofacial tardive dyskinesia, and those who scored more than 2 on any of the limb-truncal components of the AIMS. Thus, this division was hierarchical, with limb-truncal movements taking precedence over orofacial movements.

Differences between these three groups in demographic and treatment variables were assessed by one-way analysis of variance. The cognitive and negative symptom variables were investigated by one-way multiple analysis of covariance (MANCOVA), in which age, drug-induced parkinsonism, and akathisia scores served as the covariates, and by chi-square tests with Yates's correction when appropriate for dichotomous variables.

RESULTS

The demographic and treatment variables are shown in table 1. There were modest differences between the groups in age and length of hospitalization. There were significant differences between the groups in drug-induced parkinsonism and akathisia ratings. Limb-truncal dyskinetic movements were found in 24% of the patients. This rate is higher than that reported in some (21, 22) but not all (23) studies. The limb-truncal and orofacial groups did not differ in total AIMS scores (mean=10.3, SD=4.9, versus mean=12.5, SD=7.4) or in the global severity score (mean=2.9, SD=0.6, versus mean=3.1, SD=0.4).

There were significant differences between the three groups on MANCOVA (Wilks's lambda=0.71, p=0.02). Post hoc Spjotvoll and Stoline (24) tests were then per-

TABLE 1 (continued)

Number Currently Taking Anticholinergic Medication	Akathisia Score		Drug-Induced Parkinsonism	
	Mean	SD	Mean	SD
13	0.8	1.7	0.6	1.6
7	1.5	2.2	2.9	3.1
9	6.1 ^c	4.8	2.7 ^d	3.5

formed, and the results are shown in table 2. This revealed a consistent difference between the limb-truncal and comparison groups only, with the limb-truncal group being more cognitively impaired and scoring higher on the Scale for the Assessment of Negative Symptoms total and all of the subscales. The orofacial dyskinesia group differed significantly from the non-dyskinetic group only in scores on the Scale for the Assessment of Negative Symptoms total and attention subscale.

We wished to investigate whether the "limb" or "trunk" component of the limb-truncal score had different associations with the cognitive and psychopathological variables. Within the dyskinetic subjects, both the lower limb (Spearman's $r = -0.34$, $df = 47$, $p < 0.05$) and trunk ($r_s = -0.35$, $df = 47$, $p < 0.05$) AIMS scores were significantly negatively correlated with the Mini-Mental State examination score. Similarly, both the lower limb ($r_s = 0.39$, $df = 47$, $p < 0.02$) and trunk ($r_s = 0.43$, $df = 47$, $p < 0.01$) scores had significant positive correlations with the total score on the Scale for the Assessment of Negative Symptoms.

DISCUSSION

After correction for age, drug-induced parkinsonism, and akathisia, limb-truncal tardive dyskinesia was found to be associated with greater cognitive impairment and more severe negative symptoms than was orofacial dyskinesia.

One obvious difficulty with this study lies in the problem of separating the different movement disorders. This is especially difficult with limb-truncal dyskinesia and pseudoakathisia. It is possible that pseudoakathisis movements were erroneously ascribed to limb-truncal dyskinesia. There is not a rich literature on the psychopathological correlates of pseudoakathisia, but one report has found an association with negative symptoms (10). This relationship may, therefore, confound any possible association between limb-truncal movements and negative symptoms.

We chose to tackle this problem in several ways. We used as signs of akathisia patterns of abnormal move-

ments that have been suggested to be discriminating for this condition (16). Despite this, there remained a significant correlation between the akathisia and limb-truncal scores ($r_s = 0.33$, $df = 83$, $p = 0.002$). Thus, the akathisia score accounted for approximately 10% of the variance of the limb-truncal score. Therefore, in the analysis, we used the akathisia score as a covariate to try to minimize its impact as a confounding variable.

The hierarchical nature of the classification of dyskinetic status may cause problems. This approach had to be adopted because very few ($N = 4$) subjects had purely limb-truncal dyskinesia. Thus, the orofacial group had little or no limb-truncal movements, but most ($N = 16$) of the limb-truncal group had orofacial movements. It could, therefore, be argued that our findings merely reflected a relationship with the total severity of dyskinesia, rather than showing any topographic specificity. However, the orofacial and limb-truncal groups did not differ significantly on either total AIMS score or global severity scores.

All of the subjects were currently receiving antipsychotic drugs. It would, however, have been neither practicable nor ethical to withdraw this medication. This raises the possibility that some subjects may have received an erroneous dyskinetic classification. Thus, following recent increases in medication, dyskinetic movements may have been masked. Similarly, those subjects whose antipsychotic medication had been recently reduced may have exhibited a withdrawal dyskinesia. All subjects were, therefore, required to have had no drug changes in the preceding month. This requirement was easily met; only five had had changes within 3 months, and 52 had had no alterations in the preceding year.

Neither the akathisia scoring nor the rating of the Scale for the Assessment of Negative Symptoms scores was undertaken in a manner that was blind to the patients' dyskinetic status. This would, however, have been impracticable because of the overt nature of the dyskinetic movements.

This study was cross-sectional in nature and performed on an atypical group of chronic schizophrenic inpatients. Therefore, extrapolation to other populations has to be undertaken with care.

There is some evidence of caudate pathology in tardive dyskinesia. Caudate abnormalities have been reported in neuropathological (25), pneumoencephalographic (26), CT scan (27), and magnetic resonance imaging scan (28) studies. There is one report that subjects with limb-truncal dyskinesia have a greater degree of caudate atrophy than those with orofacial tardive dyskinesia (29). This finding is in keeping with the suggestion of Lohr and colleagues that limb-truncal dyskinesia may be associated with widespread loss of the numerically common γ -aminobutyric acid-releasing Spiny 1 neurons in the neostriatum (9). They also suggested that damage to the numerically less common cholinergic Spiny 11 cells would result in orofacial dyskinesia, little CT scan evidence of caudate atrophy, and only little cognitive impairment. Consistent also with this,

TABLE 2. Scores of Schizophrenic Patients With and Without Dyskinesia on the Mini-Mental State and Scale for the Assessment of Negative Symptoms

Group	N	Mini-Mental State ^a		Scale for the Assessment of Negative Symptoms											
				Total ^b		Affective Blunting ^c		Alogia ^d		Avolition ^e		Anhedonia ^c		Attention ^f	
		Mean	SD												
No dyskinesia (comparison group)	45	24.5	4.4	15.9	12.1	6.1	4.7	2.9	3.7	2.3	2.3	3.1	4.6	1.4	2.9
Orofacial dyskinesia	19	22.2	4.4	28.6	19.6	10.4	7.7	5.6	4.7	4.5	5.1	6.6	6.4	4.6	4.8
Limb-truncal dyskinesia	20	20.4	5.9	38.5	20.4	11.8	7.5	7.2	5.2	6.7	4.1	7.9	4.4	6.0	3.8

^aSignificant difference between comparison and limb-truncal dyskinesia groups ($p=0.02$; all comparisons by Spjotvoll and Stoline post hoc tests).

^bSignificant difference between comparison and orofacial dyskinesia groups ($p=0.05$) and comparison and limb-truncal dyskinesia groups ($p=0.0002$).

^cSignificant difference between comparison and limb-truncal dyskinesia groups ($p=0.01$).

^dSignificant difference between comparison and limb-truncal dyskinesia groups ($p=0.009$).

^eSignificant difference between comparison and limb-truncal dyskinesia groups ($p=0.0007$).

^fSignificant difference between comparison and orofacial dyskinesia groups ($p=0.03$) and comparison and limb-truncal dyskinesia groups ($p=0.0007$).

Klawans and Rubovits (30) found that cholinergic agents improved orofacial tardive dyskinesia to a much greater degree than limb-truncal dyskinesia.

Mukherjee et al. (29) found that subjects with limb-truncal dyskinesia also had greater frontal blood flow, as assessed by single photon emission computed tomography, than those with orofacial tardive dyskinesia. This may be analogous to the reported greater frontal blood flow in those with Huntington's chorea (31). This may be due to an "outflow obstruction" of the main efferent pathways from the frontal lobes in the caudates (31).

Limb-truncal dyskinesia is important by virtue of its relative frequency and the severity of its cognitive and psychopathological sequelae. Its study appears to have been adumbrated by that of orofacial dyskinesia. This is despite the early comment of Delay and Deniker that orofacial dyskinesia was the "most common and least worrying" movement syndrome. However, they also noted that "choreic movements of the limbs are very variable and difficult to classify" (32). Although it is difficult to assess, we would conclude that limb-truncal dyskinesia merits further study.

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The Impact of Antipsychotic Drug Regulations on Psychotropic Prescribing Practices in Nursing Homes

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The authors prospectively studied psychotropic prescribing practices and quality assurance data in 17 nursing homes in the Baltimore area to assess the impact of federal antipsychotic drug regulations. There was a 36% reduction in prescriptions for neuroleptics over 6 months, no increase in prescriptions for sedative/hypnotics, and a small increase in prescriptions for antidepressants. The authors conclude that psychotropic drug prescribing practices and patient outcomes remain important areas of study in nursing homes.

(Am J Psychiatry 1992; 149:1390-1392)

Neuroleptic drugs are frequently prescribed in nursing homes, and the particular ones used are often not optimal for elderly patients (1, 2). In a recent study of 454 nursing home patients (3), we found that 34% of patients who had dementia without delusions or hallucinations received neuroleptics, as did 24.1% of primarily depressed patients without dementia and 6.7% of patients with no psychiatric diagnosis at all.

Recognition of the data on use of neuroleptic drugs and recommendations from the Institute of Medicine resulted in federal legislation restricting the use of neuroleptics and restraints in nursing homes (the Omnibus Reconciliation Act, or OBRA, of 1987), which went into effect in October 1990. Prescribing a neuroleptic now requires specific diagnoses and behavioral indications. Garrard et al. (4) found that had OBRA regula-

tions been in effect from 1976 to 1985, 50% of neuroleptic use in almost 9,000 nursing home patients would have been out of compliance.

The impact of the new regulations has not yet been assessed. Whether they will result in less neuroleptic use or more use of other psychotropic medications or physical restraints is not known. For this study we evaluated psychotropic drug prescribing practices longitudinally for the 3 months before and the 3 months after October 1990, when the regulations went into effect, in 17 community nursing homes in Maryland. Over this time period, a pharmacist-sponsored education program for physicians and nurses was implemented. We also evaluated changes in use of restraints and in nursing home quality assurance reports to estimate possible clinical consequences.

METHOD

All 17 Baltimore-area nursing homes owned by Meridian Healthcare participated in the study. They were licensed as intermediate/skilled care facilities and ranged in size from 104 to 250 beds. Patients were admitted from the mainly white (81%-84%) and middle-income communities surrounding each home. There were 2,709 patients in the 17 homes.

Computerized monthly pharmacy reports were reviewed from July to December 1990 to determine the

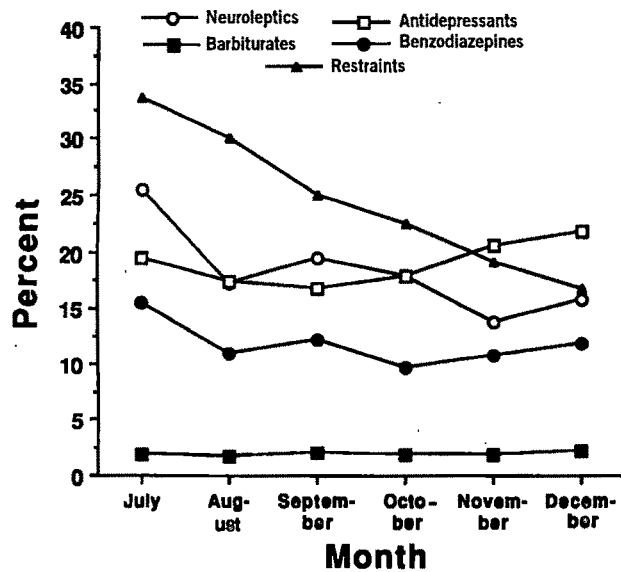
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FIGURE 1. Use of Psychotropic Drugs (N=2,707) and Restraints (N=1,923) for Residents of 17 Nursing Homes in July–December 1990



proportion of patients for whom all neuroleptics, benzodiazepines, antidepressants, or barbiturates were prescribed. To determine whether the patients who received neuroleptics throughout the study period had dose changes, only prescriptions of haloperidol and thioridazine were reviewed. These two neuroleptics were considered representative of others because they are most often prescribed in nursing homes (4). Nursing quality assurance data for 12 of the 17 nursing homes, involving 1,963 patients, were reviewed and included information on use of restraints, bedsores, weight loss (3–5 lb/30 days), falls with fractures, adverse incidents such as falls without injuries, urinary tract infections, and deaths. Five of the 17 homes were unable to provide these data, but they did not differ from the other homes in other respects.

To test for the significance of changes over time, a normal-deviate or *z* test for linear trends in proportions was used (5). To test for differences in restraint use, a *t* test was used.

In January 1990 the Meridian pharmacy service mailed the OBRA regulations to all medical directors, primary care physicians, and directors of nursing. In May 1990 all 17 nursing homes completed an assessment form recording indications for restraint and neuroleptic use, their potential side effects, and the required physician evaluations. In July 1990, the pharmacy service sponsored in-service education for nurses and physicians on proper indications, recognition of side effects, and appropriate documentation of these treatments. The pharmacy service subsequently reviewed medical records and determined whether appropriate indications were recorded. In September 1990, pharmacists asked physicians to reevaluate patients who were receiving neuroleptics or restraints without appropriate documentation.

TABLE 1. Prevalence of Medical Events Among 1,923 Residents of 17 Nursing Homes in July and December 1990

Medical Event	Period Prevalence (%)		z	p
	July	December		
Bedsores	4.8	3.3	-3.33	<0.0005
Weight loss	4.0	3.2	-1.87	n.s
Falls with fractures	0.2	0.4	1.28	n.s
Adverse incidents	12.0	14.0	3.75	<0.0001
Urinary tract infections	3.2	4.0	2.18	<0.05
Deaths	0.7	1.1	1.95	<0.05

RESULTS

Complete demographic and medical data on the 2,707 patients were unavailable; however, we studied a subgroup of patients in eight of the homes (N=454) (3) and found them to be comparable to patients in the 1985 National Nursing Home Survey (6).

In July 1990, 15.4%–45.0% (mean=25.4%, SD=7.2%) of patients in the 17 homes received neuroleptics. Figure 1 shows the use of psychotropic drugs and restraints by month in July–December 1990. Over this interval there was a marked overall decrease in prescriptions of neuroleptics from 25.4% to 15.9% ($z=-9.72$, $p<0.0001$). The magnitude of the decrease ranged in the 17 nursing homes from 9.9% to 65.6% (mean=36.1%, SD=19%) but was unrelated to the July 1990 rates ($r=0.36$, $df=20$, $p=0.16$). For patients who received haloperidol or thioridazine throughout the study period (N=135), 71 (52.6%) had no change in dose, 52 (38.5%) had their doses reduced, and 12 (8.9%) had their doses increased. There was a slight increase in prescriptions of antidepressants from 19.4% to 21.9% ($z=3.68$, $p<0.001$), a decrease in prescriptions of benzodiazepines from 15.4% to 11.9% ($z=-4.02$, $p<0.001$), and a slight change in prescriptions of barbiturates from 2.0% to 2.3% ($z=0.87$, n.s.). The proportion of patients for whom restraints were prescribed decreased from 33.6% (range=12%–73%) in July 1990 to 15.7% (range=5%–25%) in December 1990, a 53.3% reduction ($t=5.39$, $df=9$, $p<0.0001$).

Table 1 shows the prevalence of medical events reported in quality assurance reports in July and December 1990. There was a slight decrease in bedsores and slight increases in adverse incidents, urinary tract infections, and deaths. There were no changes in weight loss or falls with fractures.

Psychotropic drug use was reassessed in October 1991. The proportion of patients receiving neuroleptics was 13.5%, antidepressants 18.6%, benzodiazepines 14.7%, and barbiturates 2.0%.

DISCUSSION

We prospectively studied psychotropic prescribing practices in a large sample of community nursing home patients in Maryland. The characteristics of the patients

and the homes were similar to other for-profit community nursing homes in the United States (3). The corporation that owns the homes developed an active pharmacy program to meet the new federal antipsychotic drug and restraint regulations. This included in-service education for nurses and physicians and notifying physicians of drug and restraint regimens potentially out of compliance.

We found considerable reductions in neuroleptic use over the 6-month study period, no increase in use of sedatives/hypnotics, and a slight increase in use of antidepressants. One year later, the lower level of neuroleptic use was sustained and no increases in other psychotropics were observed. The maintenance of a lower level of neuroleptic use is probably attributable to the ongoing requirement that physicians complete an "indications and side effects" document for all residents receiving these drugs. There were also substantial reductions in the use of physical restraints for similar reasons. The initial increase in use of antidepressants was not sustained 1 year later and likely represented expected monthly variation rather than increased treatment of depression.

Although small but significant changes were noted in the quality assurance reports we reviewed, they are difficult to interpret because comparable data from previous years are unavailable. Nevertheless, they suggest that no major deviations occurred.

This study suggests the effectiveness of a pharmacy-sponsored physician and nurse education program to meet OBRA drug and restraint regulations. Previous studies have demonstrated similar successes using educational

outreach and physician feedback, although other factors (e.g., publication of OBRA requirements in the medical literature and other physician communications) may contribute (7, 8). Taken together, these studies encourage future interventions of this kind to reduce unnecessary use of medications. In the meantime, psychotropic prescribing practices and patient outcomes remain important areas of study in nursing homes.

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Anticholinergic Effects of Drugs Commonly Prescribed for the Elderly: Potential Means for Assessing Risk of Delirium

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Anticholinergic effects of the 25 drugs most commonly prescribed for the elderly were measured by radioreceptor assay. Fourteen had detectable anticholinergic drug levels; 10 of these had levels that have been associated with impairments in memory and attention in normal elderly subjects. These data indicate that patients taking multiple medications may be at increased risk for side effects from psychotropic drugs, most of which have anticholinergic effects.
(Am J Psychiatry 1992; 149:1393-1394)

The systemic absorption of anticholinergic medications is one likely mechanism of drug-induced delirium in the elderly (1-6). Medications with anticholinergic effects are associated with delirium more commonly than is any other drug class (5). Although anticholinergic-related delirium has long been recognized (3), the full extent of this syndrome may not yet be fully appreciated. The anticholinergic effects of many drugs and their metabolites are unknown. Since most elderly patients take three or more drugs (7), many of which have known anticholinergic effects, it is possible that an anticholinergic intoxication syndrome could result from complicated medication regimens in which several medications, some or all of which have modest anticholinergic effects, are prescribed. It is possible that the net risk of anticholinergic toxicity from complicated drug-drug interactions is high, even though the patient receives no readily identifiable anticholinergic compound.

We investigated the anticholinergic effects of the 25 drugs most frequently prescribed for the elderly (8). This is the first study in which these drugs have been investigated in the same assay system and the antimuscarinic effects tabulated. While some of the drugs are typically associated with anticholinergic side effects, others (e.g., warfarin) are not.

METHOD

We obtained from pharmaceutical companies, listed in the *Physicians' Desk Reference*, samples of parent

compounds of the 25 medications most commonly prescribed for elderly patients (according to the Health Care Financing Administration's initial listing of 225 drugs) (8). The anticholinergic effects of a standard concentration (10^{-8} M) of each compound were assessed in an anticholinergic radioreceptor assay (9-12). The details of this antimuscarinic radioreceptor assay have been published elsewhere (2, 10, 11). Each medication was diluted to the 10^{-8} M concentration, and anticholinergic drug levels were compared to an internal standard of atropine sulfate. So that drug levels could be compared using a uniform unit of measure, each level was then expressed as nanograms per milliliter of equivalent amounts of atropine (atropine equivalents).

RESULTS

Table 1 presents the anticholinergic drug level associated with a 10^{-8} M concentration of each compound in the radioreceptor assay (9, 10). Of the 25 most commonly prescribed drugs for the elderly, 14 produced detectable anticholinergic effects. Ten of these (ranitidine, codeine, dipyridamole, warfarin, isosorbide, theophylline, nifedipine, digoxin, Lanoxin, and prednisolone) produced anticholinergic levels that have been shown to cause significant impairments in tests of recent memory and attention in normal elderly control subjects (11).

DISCUSSION

Our results show that many medications commonly prescribed for the elderly have detectable anticholinergic effects and thus may contribute to an anticholinergic intoxication syndrome. While it is known that some compounds have anticholinergic effects, this is the first report identifying the relative anticholinergic effects of commonly prescribed agents in the same assay. Most of

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TABLE 1. Anticholinergic Drug Levels in 25 Medications Ranked by the Frequency of Their Prescription for Elderly Patients

Medication ^a	Anticholinergic Drug Level (ng/ml of atropine equivalents)
1. Furosemide	0.22
2. Digoxin	0.25
3. Dyazide	0.08
4. Lanoxin ^b	0.25
5. Hydrochlorothiazide	0.00
6. Propranolol	0.00
7. Salicylic acid	0.00
8. Dipyridamole	0.11
9. Theophylline anhydrous	0.44
10. Nitroglycerin	0.00
11. Insulin	0.00
12. Warfarin	0.12
13. Prednisolone	0.55
14. Alpha-methyldopa	0.00
15. Nifedipine	0.22
16. Isosorbide dinitrate	0.15
17. Ibuprofen	0.00
18. Codeine	0.11
19. Cimetidine	0.86
20. Diltiazem hydrochloride	0.00
21. Captopril	0.02
22. Atenolol	0.00
23. Metoprolol	0.00
24. Timolol	0.00
25. Ranitidine	0.22

^aAt a 10⁻⁸ M concentration.^bA digoxin compound.

these drugs are not typically identified as anticholinergic, and the net effect of combinations of these drugs is also generally not associated with anticholinergic toxicity. As a means of comparison, in a related study of patients in a nursing home population (12), drug levels in excess of 0.83 ng/ml of atropine equivalents were shown to have a significant effect on the capacity for self-care of elderly, largely demented subjects. The levels we found are likely to underestimate the antimuscarinic effects of these medications in patients, since potentially active metabolites of each parent compound were not assayed.

Clinicians will readily appreciate that many of their elderly patients are prescribed several of these medications simultaneously. This report should serve as a warning to psychiatrists that the addition of any medi-

cation to an already complicated medication regimen, especially that of an elderly patient, carries with it the potential risk of adversely affecting cognition in the patient. This is particularly worrisome when antidepressants or antipsychotic medications with established anticholinergic effects are prescribed. A record of all medications should be carefully obtained, and attention should be given to possible multiple drug interactions. These data may serve to alert the clinician to possible toxic drug combinations. Perhaps, by using alternative drugs, multiple anticholinergic compounds can be avoided. In instances in which an elderly patient is likely to encounter anticholinergic effects of multiple medications, the patient should be examined carefully and often for signs of anticholinergic toxicity.

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Comparison of Fluorescent Polarization Immunoassay and Radioimmunoassay in Measuring Cortisol Levels in Prepubertal Depressed Children

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Cortisol levels of 21 hospitalized prepubertal depressed children given the dexamethasone suppression test (DST) were measured by radioimmunoassay and by fluorescent polarization immunoassay, a new assay method. Correlation analyses demonstrated a highly significant linear relationship between the two methods of measuring cortisol. Thus, it may be possible to use fluorescent polarization immunoassay to measure cortisol levels in children undergoing the DST.
(Am J Psychiatry 1992; 149:1395-1396)

To perform a dexamethasone suppression test (DST) successfully, it is critical that cortisol levels be measured accurately at low plasma concentrations (1-4). The two most commonly used assay methods for determining plasma or serum cortisol levels have been competitive protein-binding assay and radioimmunoassay.

Ritchie et al. (5) reported that radioimmunoassay was the preferred method because it was easy to perform, highly specific, and low in cost. However, different antibodies may be used in the assay, and the method of separating bound from free steroids varies among laboratories. For these reasons, the results of different commonly used commercial radioimmunoassay kits are not always consistent. The APA Task Force on Laboratory Tests in Psychiatry (6) reported that commercially available radioimmunoassay kits yield inconsistent assay values for the same sample, and the same assay method can be inconsistent over time (5, 7).

The competitive protein-binding assay uses human cortisol-binding globulin as the primary binder for cortisol (5). This method can accurately measure relatively low levels of cortisol with good reliability and sensitivity. However, the competitive protein-binding assay is not completely specific for cortisol. Furthermore, this assay must be performed carefully to obtain adequate accuracy and precision, especially at low concentrations of cortisol (0-10 µg/dl), which are critical for the DST (5).

Recently, a nonisotopic immunoassay for cortisol was introduced. This new assay uses fluorescent polarization immunoassay technology. It is highly sensitive and specific for cortisol. Furthermore, it does not use

radioactive isotopes (8). The purpose of the current study was to compare the new fluorescent polarization immunoassay with the more widely used radioimmunoassay for measuring plasma cortisol levels in prepubertal children undergoing a DST.

METHOD

The subjects were 21 consecutively hospitalized prepubertal children (Tanner stage I), aged 6-12 years, who met the *DSM-III-R* criteria for major depression. There were 16 boys and five girls. All underwent a DST as part of their clinical evaluation. The DST was performed under conditions that have been previously described (9).

Baseline cortisol levels were measured at 8:00 a.m. and 4:00 p.m. At 11:00 p.m. the same day, a 0.5-mg oral dose of dexamethasone was given. Cortisol levels were then measured the next day at 8:00 a.m. and 4:00 p.m.

Serum cortisol levels were determined by means of the split-sample duplicate determination method with both a radioimmunoassay kit (Serono Laboratories, Inc., Braintree, Mass.) and a fully automated fluorescent polarization immunoassay using the Abbott Tdx fluorescence polarization analyzer (Abbott Laboratories, North Chicago). Assays were done individually as they were ordered clinically. Not all subjects had cortisol values from both radioimmunoassay and fluorescent polarization immunoassay at all four time points, as indicated in table 1.

RESULTS

Pearson correlation coefficients were calculated to determine the association between radioimmunoassay and fluorescent polarization immunoassay cortisol val-

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TABLE 1. Correlations of Cortisol Values Determined by Radioimmunoassay and by Fluorescent Polarization Immunoassay at Four Time Points for 21 Prepubertal Children Given the DST

Condition and Time of Sampling	Range of Cortisol Values ($\mu\text{g/dl}$)		Analysis		
	By Radioimmunoassay	By Fluorescent Polarization Immunoassay	r	df ^a	p
Predexamethasone					
8:00 a.m.	7.2–22.1	6.8–22.4	0.86	19	<0.0001
4:00 p.m.	2.2–11.9	2.1–17.1	0.92	14	<0.0001
Postdexamethasone					
8:00 a.m.	0.2–14.2	0.5 ^b –12.4	0.98	17	<0.0001
4:00 p.m.	0.4–18.5	0.5 ^b –18.2	0.98	15	<0.0001

^aNot all data points were available for all subjects.

^bLevels reported as <1.0 were recorded as 0.5 for the purpose of statistical calculations.

ues at each of the four time points (table 1). Correlations at each of the four sampling times were highly significant.

To determine whether the degree of correlation between radioimmunoassay and fluorescent polarization immunoassay was in some way affected by cortisol values that were either high or low, cortisol levels were divided into high ($>8 \mu\text{g/dl}$), medium ($\geq 3 \mu\text{g/dl}$ to $\leq 8 \mu\text{g/dl}$), and low ($<3 \mu\text{g/dl}$) categories. Correlations were then calculated for cortisol levels obtained within these categories at each of the four sampling times. This was done to maintain independence of analyses for repeated measures. At least five paired observations were required for statistical analyses; thus, only six of 12 comparisons were analyzed. All correlations were significant (for high cortisol values: 8:00 a.m. baseline, $r=0.81$, $df=18$, $p<0.0001$; 8:00 a.m. postdexamethasone, $r=0.91$, $df=4$, $p<0.03$; for medium values: 4:00 p.m. baseline, $r=0.88$, $df=11$, $p<0.0002$; 4:00 p.m. postdexamethasone, $r=0.92$, $df=5$, $p<0.01$; for low values: 8:00 a.m. postdexamethasone, $r=0.64$, $df=12$, $p<0.02$; 4:00 p.m. postdexamethasone, $r=0.90$, $df=8$, $p<0.001$).

With $5.0 \mu\text{g/dl}$ as the cutoff value for nonsuppression of cortisol, we used chi-square analyses to compare the sensitivities of the radioimmunoassay and the fluorescent polarization immunoassay in interpreting the DST. The results were highly significant ($\chi^2=65.01$, $df=1$, $p<0.0001$), with 71 of 73 cortisol levels in agreement. For 27 levels, both assays indicated a negative DST result (i.e., $<5 \mu\text{g/dl}$). For 44 levels, both assays indicated a positive DST result (i.e., $>5 \mu\text{g/dl}$). Finally, in two instances, the radioimmunoassay levels showed negative results (4.40 and $4.80 \mu\text{g/dl}$) while the fluorescent polarization immunoassay levels showed positive results (5.50 and $5.00 \mu\text{g/dl}$, respectively).

DISCUSSION

In this study, cortisol levels determined by fluorescent polarization immunoassay and by radioimmunoassay were highly correlated. This correlation was consistent at varying absolute cortisol levels. To our knowledge, there are no similar studies of children for comparison. Ritchie et al. (8) compared plasma cortisol levels in 169

postdexamethasone samples by using fluorescent polarization immunoassay and competitive protein binding. Cortisol values determined by the two methods were highly correlated; however, all 62 subjects were adults.

Although preliminary, this study suggests that it may be possible to use fluorescent polarization immunoassay to measure cortisol levels in prepubertal depressed children undergoing a DST. A $5 \mu\text{g/dl}$ cutoff value for the fluorescent polarization immunoassay method provided results comparable to those obtained with the same value for the radioimmunoassay method. However, the question of whether the variability of fluorescent polarization immunoassay is comparable to the interest and interkit variability of radioimmunoassay is left unanswered. Thus, replication and further study are indicated.

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Book Forum

Nancy C. Andreasen, M.D., Ph.D., Editor

GENERAL REVIEW

Review of General Psychiatry, 3rd ed., edited by Howard H. Goldman, M.D., M.P.H., Ph.D. Norwalk, Conn., Appleton & Lange, 1992, 481 pp., \$29.50 (paper).

The *Review of General Psychiatry* has become a popular educational tool in courses for medical students. This third edition follows a first (1984) and second (1988). Each chapter has been thoroughly updated without sacrificing the brevity and conciseness the editor promises his readers. Five chapters that are new to this edition include an outstanding one, "Group Psychotherapy" by Nick Kanas, who also contributes the excellent chapter on alcoholism.

The book has four main sections: Theory and Concepts, chapters 1 to 8; Psychiatric Assessment, chapters 9 to 15; Mental Disorders, chapters 16 to 30; and Treatment Modalities, chapters 31 to 43, which includes the topics of behavioral medicine, caring for the chronically ill and dying patient, geriatric psychiatry, consultation-liaison psychiatry, forensic psychiatry, and emergency psychiatry.

There is also a glossary of psychiatric signs and symptoms that is slightly more than four pages in length. It is the one portion of the book where brevity creates a disadvantage, and since it is followed by an unusually complete index of 14 pages it is difficult to understand how the glossary would be of much help to medical students. It might better have been placed with the chapter on the mental status examination because it confines itself to signs and symptoms, but even there it would need reworking to include some of the phenomena considered important enough to be boldfaced in the text, such as coma, somnolence, lethargy, vigilance, comprehension, constructional ability, and abstraction.

The high quality maintained in the rest of the book more than compensates for any lack in the glossary. The authors, almost without exception, have clearly made a special effort to address medical students in language familiar to them. In "Personality Disorders," for example, Charles Marmar considers each disorder as it might appear in medical practice, how it affects treatment and the patient/doctor relationship, and what might be a useful tack to take in approaching a patient with that disorder. In a table of defense mechanisms, David Preven and James David define "sublimation" as redirection of an unacceptable impulse into an acceptable form of behavior: an individual with intense unconscious voyeuristic impulses becomes a sex therapist.

Throughout the book, good use is made of clinical vignettes. Dr. Goldman introduces the section on psychiatric assessment with a two-page character sketch of "The Mayor of Wino Park." He ends the section with an eight-page clinical case summary of the "mayor" that demonstrates how the material in the assessment section is applied to an actual case.

Review of General Psychiatry is a first-rate achievement. It should be welcomed by every instructor of psychiatry in medi-

cal schools and by any psychiatrist who tries to describe the biopsychosocial perspective.

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PSYCHOPHARMACOLOGY

The Practitioner's Guide to Psychoactive Drugs, 3rd ed., edited by Alan J. Gelenberg, Ellen L. Bassuk, and Stephen C. Schoonover. New York, Plenum, 1991, 504 pp., \$37.50.

This soft-covered text is a meaningful attempt to provide information to the practicing physician about psychoactive drugs. It often gives some background information about psychiatric disorders before discussing the treatment of these disorders. Such information may be especially useful to primary care physicians or medical trainees. The table of contents reveals an ambitious array of topics, including some not always covered in a psychopharmacology text, such as insomnia, use of psychotropics during pregnancy, and pediatric and geriatric psychopharmacology.

The book is multiauthored and has some unevenness in quality. The chapters covering the treatment of major psychiatric disorders such as mood, anxiety, and psychotic disorders are nicely done and present substantial clinical material that is very useful. (Where else can a busy clinician find a list of 11 saliva substitutes for anticholinergic dry mouth?) Contrarily, some chapters seem to lack scientific rigor at times. For example, the discussion of benzodiazepine abuse suggests that tolerance develops to the anxiolytic effects, leading to increases in dose. Although an occasional patient with anxiety disorder may need a slight dose adjustment, there is no good evidence that anxiolytic tolerance develops in most appropriately selected patients with anxiety.

Another occasional problem is that some tables appear to be so overinclusive that they lose their intended usefulness. The table on organic causes of depression lists 66 disorders, including diseases such as brucellosis. (You may want to quiz your colleagues about the possibility of brucellosis in your next febrile depressed patient.) Similarly, table 12 lists many medications that may be "associated" with but not necessarily "causative" of depression. How good are the data that led to placing many of these medications on this list? Without detailed discussion, this information may create more confusion than enlightenment.

The chapter on psychotropic treatment during pregnancy presents a useful review. This chapter and divine guidance can help the physician treat these challenging patients.

The discussion about insomnia covers a topic that concerns many patients and physicians but, unfortunately, not enough researchers. The author suggests that there are conflicting data about whether antihistamines are useful for insomnia. He also states that there is little evidence that over-the-counter hypnotics are more effective than placebo.

This book should be considered by physicians or medical trainees who want a respectable overview of psychotropic medications. It measures 9 by 7 inches, thereby fitting into an extra large white coat pocket. However, its more than 500 pages will give the coat a slight list to starboard.

MICHAEL J. GARVEY, M.D.
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Manual of Clinical Psychopharmacology, 2nd ed., by Alan F. Schatzberg, M.D., and Jonathan O. Cole, M.D. Washington, D.C., American Psychiatric Press, 1991, 352 pp., \$35.00 (spiral-bound).

One of the defining roles of a psychiatrist is the prescribing of psychotropic drugs. The medical profession and the public expect psychiatrists to be experts in this area. Therefore, it is important for psychiatrists to have a solid base of information on psychopharmacology and to build on this base with clinical experience, discussions with colleagues, and regular doses of self-education through reading journals, newsletters, and books. The problem with books in fulfilling this function is that they are often dry renditions of studies that do not reflect actual clinical practice and challenges. The book under review attempts to avert this problem and "to provide the reader/practitioner with basic and practical information regarding the many classes of psychiatric medications" (p. 3). The authors set out to accomplish this by "drawing on our own clinical experience as well as the scientific literature" and not by recounting "a series of meticulously documented review papers" (p. 3).

The authors succeed in providing a readable, useful review of psychopharmacology for the clinician. The book has a conversational tone and reads as if one were listening to expert colleagues chatting about their current opinions regarding the use of psychotropic drugs. This tone is embedded in clear, logically structured chapters, covering antidepressants, antipsychotics, mood stabilizers, antianxiety agents, hypnotics, and stimulants. In addition, there are chapters on combination treatments, emergency room treatments, and pharmacotherapy of chemical dependence and special situations (pregnancy, geriatric patients, medical conditions, etc.). There is also a chapter on general principles of psychopharmacological treatment (which concentrates mainly on informed consent and Food and Drug Administration issues) and one on the diagnosis and classification of psychiatric disorders that is, however, too superficial for clinicians and probably even residents and should be either expanded or deleted.

An annoying aspect of the book's format is that the authors reference few of their statements, choosing to place an extensive bibliography at the end of each chapter. This is not a problem when the authors clearly label a statement as resulting from their clinical experience, such as, "We have recently become impressed by the number of acutely psychotic patients who show little response to relatively high doses of perphenazine and have been using the drug less often in manic and schizophrenic patients" (p. 101). However, if a reader wishes to pursue a particular statement to its source or wishes to check when or where a study was published or who did it, he or she is faced with attempting to find it in the lengthy bibliography. Sometimes it is not clear if a statement is from the authors' clinical experience or from a study, e.g., "One notable exception [to the rule that antidepressants take 2 weeks to work] is amoxapine, which may work in as little as 4 days and enjoys a claim for more rapid onset" (p. 42) or, "Meprobamate is, in fact, an effective antianxiety agent in the same sense

that diazepam or chlordiazepoxide is effective, although controlled studies directly comparing the efficacy of meprobamate with benzodiazepines are almost nonexistent" (p. 209). The authors are also inconsistent, occasionally referencing a particular statement (although not often) and referencing some tables but not others.

There are several omissions from the book that weaken its general usefulness. In the chapter on hypnotics, there is no discussion of attempting sleep hygiene methods before giving a hypnotic. There is little to no information in the book either noting the lethal doses of medications or describing the symptoms or treatment of overdoses. This is especially surprising given that the authors appropriately advise that psychiatrists should call emergency room physicians when overdoses occur because "emergency room physicians may know less about the pharmacological effects of psychiatric drugs than they [psychiatrists] do" (pp. 289-290). This manual, however, gives no information regarding the management of the overdose itself and would thus not allow the psychiatrist to help out the emergency room physician. Finally, although there is occasional mention in the chapters regarding costs, there is insufficient discussion of the relative costs of psychiatric drugs and the manner in which this should be factored into decisions regarding prescribing. Although there is a table in the appendix listing the price of medications, it is incomplete, leaving out benzodiazepines, hypnotics, mood stabilizing agents, and stimulants.

Overall, this manual's strengths outweigh the relatively minor weaknesses noted. It is written in a clear conversational style by two acknowledged experts in psychopharmacology who are sensitive to the fact that clinicians have to make decisions regarding patients despite an incomplete data base in the scientific literature to support them. These authors give such clinicians clear, up-to-date, and rational guidelines on how to proceed given this ambiguity by reviewing the available literature and conveying the knowledge they have gained through their extensive clinical experience. Absorbing the contents of this book will allow clinicians to develop the expertise in psychopharmacology expected of them by their medical peers and the public.

BARRY LISKOW, M.D.
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What You Need to Know About Psychiatric Drugs, by Stuart C. Yudofsky, M.D., Robert E. Hales, M.D., and Tom Ferguson, M.D. Washington, D.C., American Psychiatric Press, and New York, Grove Weidenfeld, 1991, 619 pp., \$35.00.

Consumers have been legitimately concerned about the possible hazards of medication, and it seems that, of late, increasing concern has been expressed about psychiatric drugs. Articles in magazines and newspapers regarding Prozac (fluoxetine) and Halcion (triazolam), for example, assault the consumer and patient with the potential horrors of psychiatric medication. Members of the antipsychiatric establishment commonly accuse psychotropic drugs of producing both long-term and short-term damage. However, there is relatively little objective information available to consumers and patients, outside of standard home medical care guides and the psychiatric drug guide published by Consumers Union. It is fitting, then, that the American Psychiatric Press published this book for the psychiatric patient regarding the drugs that form the basis of psychiatric practice.

What You Need to Know About Psychiatric Drugs admirably provides clear and accessible information about psychotropic drugs for a patient. It begins with a series of prototypical questions that a patient might ask regarding the use of psychotropic drugs and how these questions might be answered. The first half of the book then reviews drugs by their therapeutic classification. The first chapter, on antidepressant drugs, sets the model for the remainder of this section of the book. There is a very clear definition of depression and depressive symptoms, illustrated by several paragraph-long case histories of patients with the disorder. Each chapter describes the clinical use of a particular class of psychotropic drugs: antidepressants, anti-anxiety drugs, anti-panic and anti-phobic drugs, anti-manic drugs, antipsychotics, sedatives and sleeping pills, anti-addiction drugs, and drugs for attention-deficit hyperactivity disorder. Each also contains important sections about drugs that do *not* treat depression and should not be used for depression. Information on overdose and drug interactions is clearly provided. The first half concludes with chapters on drugs for dementia, for the elderly, and for anger and aggression, a chapter on ECT, and an optimistic chapter outlining the development of psychiatric drugs and treatments for the future. The writing is very clear, nonpatronizing, and designed to be accessible and helpful to the lay reader. The content is accurate, although in a few cases the lag between the writing of the book and the publication makes a few statements out of date (e.g., fluoxetine is no longer available only in 20-mg tablets but also in liquid form).

The second half of the book lists individual drugs in alphabetical order. Each drug receives 3–4 pages, and each chapter is organized similarly. The generic and brand names are given, and cross-references to drugs mentioned elsewhere in the are provided. Next, a paragraph of “fast facts” tells the reader to which class the drug belongs, whether a prescription is needed, whether it is available as a generic, and whether it is habit forming. A big white cross on a black background visually calls attention to the possibility of overdose.

Special precautions are then discussed, such as pregnancy and breast feeding, infants and children, the elderly, and driving. Reasons for not taking the medication are also given. Next, a list of benefits versus risks, prescribing guidelines, and a list of interactions with other drugs, foods, and alcohol are provided. Nondrug alternative treatments discussed elsewhere in this book are referred to, and a brief description of long-term use is provided.

In these individual drug description sections, which are generally superb, occasional information may raise questions. For example, regarding dosage of triazolam, the authors say, “A maximum daily dose of up to 0.5 mg/night may be used, if necessary.” Although this is theoretically true, some readers may interpret this as license to take 0.5 mg, when current information clearly suggests that this dose is too high except under very unusual circumstances. The habit-forming potential of triazolam is listed as high, but the risk of becoming dependent on triazolam is not discussed or placed in a risk-versus-benefit context (nor is this discussed for other benzodiazepines). It is possible, therefore, that this information might frighten some readers away from benzodiazepines or even triazolam without their clearly understanding that short-term use does not necessarily lead to dependence and that dependence, although likely after prolonged use, still, in most cases, may be mild and reversible. With fluoxetine, the other drug of current concern, one of the more common side effects (sexual dysfunction) is not mentioned, and, as already noted, the possibility of a dose less than 20 mg is not discussed.

Overall, in a large and comprehensive book such as this one,

various readers may find other small matters to quibble with, but the benefits of the book must clearly be trumpeted louder. My expectation is that this exceptionally clearly written and comprehensive volume will be very useful to patients who have concern about the drugs they may be taking or considering. It certainly is a resource for psychiatrists whose patients may ask, “What can I read about my disorder or the medication that I am taking?” For the patient who wishes to be informed, this book should have the very highest recommendation. My only concern is that, since it is written by psychiatrists and published by the American Psychiatric Press, it may be seen as self-serving by those who will look for any excuse to attack psychiatry or psychiatric medication. I hope, therefore, that the book will be distributed widely enough to be reviewed and seen by enough informed readers that its importance and usefulness will become widely known.

CARL SALZMAN, M.D.
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Child and Adolescent Clinical Psychopharmacology, by Wayne H. Green, M.D. Baltimore, Williams & Wilkins, 1991, 213 pp., \$29.00 (paper).

Last week, as my wife and I watched in awe a skilled librarian transform the congeries of 4,000 books into Dewey-decimal-ordered user-friendly rows, I could not help remembering Evaristo Zambo. When I was 12, I worshiped this Filipino conchologist, who discovered one of the world's rarest and most treasured seashells, the *Gloria maris*. When I asked him how he was able to single out that one shell when so many of us had recently combed the same beach and passed it over, he told me the origin of the word “serendipity.” He said that the secret of the success of the three princes of Serendip was in two key words: discernment and cataloging. Reading this amazing little book gave me this very same imagery. The fellowship of child psychiatrists is a small and cozy one because there are so very few of us, so I approached this book with suspicion when I read the foreword by Melvin Lewis, former editor of the *Journal of the American Academy of Child and Adolescent Psychiatry*. How could a book this small possibly live up to his almost idolatrous advanced billing? (“One might go so far as to say that no clinician should prescribe psychotropic medication for children and adolescents without having read such a book. Indeed, I can think of no other book that meets the needs of clinicians as does this one.”)

Dr. Green's work really is that good.

An associate professor of clinical psychiatry at the New York University School of Medicine and, along with his colleague Magda Campbell, recognized as an authority on child and adolescent psychopharmacology, Dr. Green gives the reader a sense of ease and familiarity as an avuncular tour guide of this infant discipline. He starts off immediately inside the front cover with a catalogue of 15 diagnoses in childhood and adolescence for which pharmacotherapy may be therapeutically indicated.

The sections entitled General Principles of Psychopharmacology With Children and Adolescents and Specific Drug Treatments should be required reading not only for all psychiatrists but also for all nurses and physicians who come in contact with any psychotropic medications. In my practice, I have come to realize that for the majority of my patients the family physician has already tried at least one psychotropic medication. The task of unraveling and teasing out the iatrogenic from the virginal disease picture becomes almost Her-

culean if not Sisyphean. Like the seasoned clinician, meticulous researcher, and skillful teacher that he is, however, Dr. Green takes us through maturational/developmental issues, relationship to the patient's family or caretakers, the process of explaining medication to the child or adolescent, medico-legal issues, baseline assessments, medicating the patient, untoward side effects, monitoring serum levels, length of time to continue medication, placebos, evaluating research studies, and specific drug treatments.

It is refreshing to hear Dr. Green expose false or dubious research. Child psychiatrists are often called on to treat patients under the age of 12 with medications that can be life-saving but are not officially recommended for these age groups because of inadequate research on children. Dr. Green says, "In evaluating the literature on child and adolescent psychopharmacology, it is important to remember that the fact that a drug is statistically significantly better than another drug or placebo does not necessarily mean that the drug is an optimal treatment for a given condition or for a specific child or adolescent. The drug may be effective only in certain environments (e.g., a laboratory) and not generalize to more ordinary circumstances, or it may improve only certain symptoms but not affect other major target symptoms to a clinically meaningful degree, or the overall improvement may be relatively modest with significant symptoms or deficits remaining."

Textbooks like this often suffer from an inescapable comparison to the television program that summarizes one day's National Football League game highlights in 3 minutes or less, something like watching a videotape of eight football games at fast forward. Such compendiums are usually encyclopedic, wobbly on supporting data, and cavalier or pompous. These criticisms do not apply here.

One of Franklin Roosevelt's favorite fantasies was spending an evening with an author and picking his brains. The reader of this book will get the sense that Dr. Green just happens to be in the neighborhood and is gladly spending that evening in an unharried, kindly, leisurely discussion of a topic he not only is inexhaustibly expert on but also hopelessly in love with.

TRUCE T. ORDOÑA, M.D.
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Neuroleptic Malignant Syndrome: A Clinical Approach, by Gerard Addonizio, M.D., and Virginia Susman, M.D. St. Louis, Mosby Year Book, 1990, 167 pp., \$35.00.

In this excellent, clinician-oriented book, the authors industriously attempt to present the controversies in the literature on neuroleptic malignant syndrome and make recommendations based on a comprehensive and critical review of all the data. The book is organized into 13 chapters, beginning with a historical perspective followed by chapters dedicated to important aspects of this potentially lethal iatrogenic illness.

The literature on neuroleptic malignant syndrome consists mostly of case reports and is replete with divergent views on almost every aspect of this illness. This includes diagnostic criteria, demographics and risk factors, pathophysiology, and treatment recommendations. Most conclusions regarding the syndrome are drawn from a series of published case reports rather than from controlled, prospective studies. The authors present the controversies in the literature in an elegant fashion, including, for example, the diagnostic criteria of Levenson versus those of Keck et al., the role of lithium in causation of the

illness, and the issue of neuroleptic malignant syndrome being a spectrum illness.

Chapter 2 is excellently written and discusses the risk factors in neuroleptic malignant syndrome, dispelling myths regarding sex and age in relation to the illness. In addition, the authors provide important information on electrolyte disturbance and organic brain syndromes as predisposing factors to this illness. I would also like to highlight the chapter on differential diagnosis, which provides a clear and succinct discussion of events that should be differentiated from this illness, such as heat stroke, malignant hypothermia, and lethal catatonias. The discussion of pathophysiology is excellent, presenting the hypodopaminergic function theory of neuroleptic malignant syndrome, muscle contraction studies, hyperadrenergic states, and the role of γ -aminobutyric acid in causation of this illness.

Some important issues related to treatment are well presented in this book, such as the initial time interval before restarting neuroleptics, type of neuroleptic to be used, and the concept of prophylaxis with bromocriptine before starting neuroleptics. The issue of prophylaxis with bromocriptine is something new I learned from this book. The authors talk about the neuroleptic malignant syndrome occurring in non-psychiatric patients, in patients receiving nonpsychiatric medications such as metoclopramide, and in patients experiencing withdrawal from antiparkinsonian agents such as levodopa.

This book is easy to read, is a source of quick reference, and has excellent summaries at the end of each chapter in addition to tables listing all case reports and studies relevant to the topic of discussion. Technically the book is of high quality with good editing; typographical errors and misspellings are rare. The bibliography gives an extensive list of references pertaining to each topic. This book will not only prove useful for psychiatrists and trainees but also serve as a source of quick reference for family physicians, physicians in emergency rooms, and physicians in intensive care units. Reading this book is strongly recommended.

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BRAIN AND BEHAVIOR

Psychopathology and the Brain, edited by Bernard J. Carroll and James E. Barrett. New York, Raven Press, 1991, 312 pp., \$131.50.

This volume was derived from proceedings of the 1989 meeting of the American Psychopathological Association, a meeting at which Walle J.H. Nauta was honored. Appropriately, the focus of the presentations concerned the brain, particularly new developments in neuroscience that provide better understanding of the brain systems involved in abnormal behavior. Five major topics—frontal/limbic/striatal mechanisms in psychosis, basal ganglia, behavioral biology and development, personality, and affective disorders—were discussed. The volume makes no attempt to cover all aspects of brain and behavior, purposefully omitting such significant areas as genetics, endocrinology, and pharmacology. Eight of the 14 chapters present data from human studies relating abnormal behavior to brain abnormality. The remaining six chapters present animal research germane to human behavior and development. Each chapter is followed by an abstracted discussion in which individuals attending the meeting com-

mented on the papers and presented questions or ideas from their own backgrounds. Many of these discussions are both lucid and helpful.

The volume covers a broad expanse of psychopathology and is dependent on one or two well-formulated presentations for each individual behavioral problem. Although not as complete as a textbook and not as current as a journal, the volume does provide an excellent overview of many of the important approaches being taken in the brain/behavior field through well-written and authoritative papers. For the individual physician or scientist interested in brain/behavior relationships but who has neither the time nor the energy to cull such information from the contemporary literature, this volume provides a superb and relatively up-to-date presentation.

D. FRANK BENSON, M.D.
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The Psychoses of Epilepsy, by Michael R. Trimble. New York, Raven Press, 1991, 210 pp., \$68.50.

The development of psychotic symptoms in epileptic patients has been reported since the earliest days of medical writing. Recently the relationship between epilepsy and psychosis has generated considerable controversy. This volume, authored by one of the world's leading authorities on the coexistence of psychosis and epilepsy, appears destined to become a definitive reference for any psychiatrist who might become involved in caring for those afflicted with both an epileptic and a psychotic disorder.

In 11 clearly written, easily read chapters the author exposes the reader to current knowledge as well as controversial issues. The book presents all the pertinent data necessary to make a clear case that epilepsy certainly can have an impact on its victims' cognitive and emotional lives.

The first chapter sails through the history of the relationship between epilepsy and psychosis from antiquity to the twentieth century. This chapter is meant for those clinicians and researchers who are interested in epilepsy and psychosis. It provides a historical framework of the evolution of the thinking of laymen, scientists, and clinicians as they accumulated factual knowledge over the years.

The second chapter discusses the usual classification of the epilepsies (available in any neurology book), as well as a classification of the possible anatomical sites of the abnormal activity that directly bear on the behavioral manifestations of the different types of seizures.

The third chapter is written for nonpsychiatrists to familiarize them with the current classification of psychiatric disorders. Chapter 4 provides an anatomical overview of the limbic system and related brain areas and is required reading for those who plan to get involved in managing psychotic patients with epilepsy. It is no secret that most psychiatrists are not well versed in neuroanatomy. I would venture to say that studying this chapter is a minimum requirement for attempting to care for patients with both epilepsy and psychosis.

The fifth chapter, "Forced Normalization and Alternate Psychosis," is a good introduction to the complex relationship between these two brain disturbances. Forced normalization has been controversial, but this chapter provides a strong argument for its validity, supported by an exhaustive review of the literature.

Chapters 6-8 provide a full clinical description of the many psychiatric symptoms that have been associated with epilepsy. These chapters are indeed the meat of the book. Along with

chapter 10, which details the management of these patients, these three chapters should be read by any practitioner who might become involved in such patients' clinical care. A chapter on postoperative psychosis and another on the risk factors for the development of epileptic psychosis qualify this volume as a comprehensive text for its topic.

I feel that all psychiatrists need at least to look at selected chapters, but the whole volume is required reading for those who are involved in daily care of the psychoses of epilepsy.

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ETIOLOGY AND NOSOLOGY

Schizophrenia Genesis: The Origins of Madness, by Irving I. Gottesman. New York, W.H. Freeman and Co., 1991, 284 pp., \$24.95; \$14.95 (paper).

Any clinician who has struggled to answer questions from patients' families such as, "Why did my son get schizophrenia?" or, "My wife's sister has schizophrenia, what chance does my daughter have of becoming ill?" will find the current work by Irving Gottesman a boon. However, *Schizophrenia Genesis: The Origins of Madness* is more than just a listing of risk tables. Cogent and engagingly written, the book not only presents the results of many studies from diverse fields but also elucidates the methods and the thinking processes that allow intelligent interpretation of their results.

The book begins with a brief review of the history of schizophrenia, including changing fashions in the concept of the disease. This leads to a discussion of the modern criteria for schizophrenia phenomenology. Dr. Gottesman then proceeds to introduce the fundamental concepts of psychiatric epidemiology. His central point is the concept of age-corrected morbid risk. He not only clearly describes this concept but explains its importance as a benchmark for comparing risk factors for schizophrenia among different studies. He then explains the basics of Mendelian inheritance.

With this groundwork, the reader is readily led through a discussion of classic family, twin, and adoption studies to the conclusion that there is indeed a familial (genetic) contribution to liability to schizophrenia but that environment influences the manifestation of this liability (the diathesis/stressor model). The next chapter describes patterns of mortality, cancer, suicide, criminality and violence, and fertility in schizophrenic patients, which leads to a discussion of public health policies and genetic counseling. Although he has previously provided rough estimates of the risk for different degrees of kinship, Dr. Gottesman emphasizes that an individualized approach to counseling is necessary for any putatively multifactorial trait such as schizophrenia. He describes computer-based risk assessment, the details of which are probably best left to professional genetic counselors. In the final chapter, Dr. Gottesman briefly touches on neurobiology to provide a "flavor" of the current efforts to understand the connection between genetic and environmental influences on the one hand and brain function on the other. He concludes with a description of molecular genetics and potential contributions from these techniques.

Some readers may object to the short shrift given neurobiology. However, the book provides a clear view of both the data and the underlying thinking that led an eminent re-

searcher in psychiatric genetics to a polygenic diathesis/stress-or theory of schizophrenia.

In addition to the wealth of data presented, the book also includes first-person accounts by patients and their families, presumably to enrich the reading experience beyond that provided by a sole discussion of clinical research results. Dr. Gottesman states that his intended audience includes the curious lay person as well as the mental health professional. In the absence of some basic background in science and mathematics, the book may be rough going. However, to any interested mental health professional, *Schizophrenia Genesis* not only provides valuable information but is enjoyable in the process.

STEVEN D. FORMAN, M.D., PH.D.
DANIEL P. VAN KAMMEN, M.D., PH.D.
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Etiology of Mental Disorder, edited by Einar Kringlen, Nils Johan Løvik, and Sverre Torgersen. Oslo, Department of Psychiatry, Vindern, University of Oslo, 1990, 211 pp., \$25.00 (paper).

This is an interesting book, in some ways quite useful and in many ways disappointing. It is a compilation of papers from an August 1990 World Psychiatric Association symposium in Oslo devoted to the topic of the title. Plenary sessions were held in the areas of schizophrenia, mood and personality disorders, child psychiatry, and senile dementia. The book itself is a compilation of several of the main papers from this meeting. Additional papers included in the volume are "Neurodevelopment and Schizophrenia" by Pilowski, Kerwin, and Murray, "A Summary of Psychiatric and Psychological Findings From the Minnesota Study of Twins Raised Apart" by Segal, Eckert, Grove, Bouchard, and Heston, and "Towards a Phenomenology of the Torture Situation" by Doerr-Zegers, Hartmann, Lira, and Weinstein. The organization of the book is quite interesting in that the papers presented at the meetings are published along with a discussion of the papers. In some cases the discussion is as informative as the papers, and in a few of the discussions the references considerably extend the main papers themselves. As with many texts that emanate from meetings, the papers are quite uneven and the volume suffers from a lack of integration. The strengths, however, are in the quality of the contributions themselves and in the presentation of some material that is not usually found elsewhere.

The first section, Child Psychiatry, consists of two papers. The first, by Steinhausen, "Etiology of Child and Adolescent Mental Disorders," is a very broad overview of the topic. Cederblad's discussion of this paper is brief but quite interesting and presents a somewhat independent view.

The second section, Schizophrenia, consists of papers by Tienari, Parnas, and Kringlen and a discussion of all three by Ciompi. The three papers relate to adoption studies, twin research, and longitudinal high-risk research, and the discussion is quite excellent and presents a model for the development of this illness.

The third section, Mood Disorders, includes a paper by McGuffin, Katz, and Bebbington on genetic transmission of mood disorders and another by Craig on the social etiology of depression. Katschnig provides a discussion of both papers. Although this section is somewhat brief there is a lot of attention to detail and the references are quite current. The exposition of genetic and environmental interactions is well done.

The fourth section, Personality Disorders, consists of a paper on the etiology of personality disorders by Torgersen and

a rather brief discussion by Reich. Torgersen's paper is a good overview of the problem with a pertinent reference list.

The fifth section, Senile Dementia, also contains one chapter, "Etiological Factors in Dementia" by Gottfries, and a discussion by Levy. Both the paper and the discussion are comprehensive.

Of the special papers included, the study on Minnesota twins raised apart was a good summary of this work.

Etiology of Mental Disorder is a paperbound book that actually took a fair amount of time to read. There are several tables and charts to illustrate overview concepts and data, and the chapters are somewhat longer than one usually expects from a symposium of this type. There are several typographical errors throughout the text. The overview by Kringlen at the beginning of the book reviews the content of each particular chapter and is quite useful.

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Problems in Differential Diagnosis: From DSM-III to DSM-III-R in Clinical Practice, by Andrew E. Skodol, M.D. Washington, D.C., American Psychiatric Press, 1989, 518 pp., \$44.00.

Psychiatric nosology is an amalgam of science, tradition, and convenience. In referring to a manual of diagnoses such as *DSM-III* or *DSM-III-R* it is difficult to know whether the source of a particular criterion is based in science, tradition, or convenience. This book is a tool to help us in that regard. The stated goals are to guide clinicians in the application of principles of differential diagnosis, place *DSM-III* and *DSM-III-R* in a clinical context, and bring together clinical and research traditions. It also serves the more important purpose of helping clinicians adapt to empirical psychiatry and has many features in its favor. All of the chapters are written by one author, which is a rarity these days. Actual case vignettes are used to discuss the *DSM* criteria, making the reading easier, but the book remains difficult to read.

There are 12 chapters, 10 devoted to syndromes and two to diagnostic interviewing and multiaxial diagnosis. The latter are the best written and contain many pearls of clinical wisdom; for example, on interview technique: "The interviewer is not considered successful if a diagnosis can be made but the patient becomes less willing to continue or seek treatment" (p. 2). It is gratifying to read that Dr. Skodol recommends a complete course in modern psychopathology as part of the training requirements for first-postgraduate-year trainees.

Several provocative statements are made, but the reader will be disappointed to find no discussion of these. To cite a few examples, regarding multiaxial diagnosis Dr. Skodol states that an axis is nothing more than a "clinical perspective" (p. 40), implying that a longitudinal/developmental perspective of hallucinations or dysphoria would make them axis II dysfunctions. In the chapter on psychosis he says without citing any literature that "hallucinations are indicative of psychosis only when the person experiencing them has no insight into their pathological nature" (p. 163). The implications of these concepts for pathophysiology and treatment are not mentioned.

The quality and depth of the discussions are variable. The problems remaining in *DSM-III-R* are fairly presented; in particular, Dr. Skodol points out where he differs from the official *DSM-III* and *DSM-III-R* versions, although he was very much a part of their development. The discussion pertaining to axes

III, IV, and V is limited. The use of axis III by nonphysicians is dealt with in one paragraph and stated to be a simple matter of recording the diagnoses made by a physician (p. 53). It is clear, however, as the author notes in his discussion of somatoform disorder (p. 336), that nonphysician clinicians are often asked to make judgments about physical disorders. As much as the criteria can be spelled out, their correct application is an issue of clinical judgment, and there is no substitute for medical training and experience in this regard. This is not brought out at all. The new convention introduced in *DSM-III-R* of rating severity is appropriately highlighted—for many years we have diagnosed patients without referring to severity—but there is no discussion of its overlap with axes IV and V or the utility of these axes. The 10 chapters on psychiatric syndromes do not have a common format, although most provide an introduction, a discussion of terminology, and an overview of the diagnostic and conceptual aspects of the syndromes. The changes from *DSM-III* to *DSM-III-R* are then critically reviewed, and a brief summary recapitulates the material.

In the chapter on organic mental syndromes, *DSM-III-R* innovations are well summarized, including the removal of the psychotic/nonpsychotic and acute/chronic dichotomies and the recognition that partial cognitive impairment is sufficient for a diagnosis of organic mental syndrome rather than the global reduction required in earlier *DSMs*. The point that organic personality syndrome is almost always from an illness intrinsic to the brain whereas organic mental syndromes could occur as a result of systemic illness elsewhere in the body is of practical utility. The table on pages 112–115 of systemic and CNS diseases that can potentially cause organic mental disorders is worth carrying in our pockets during rounds. The chapter on psychosis, on the other hand, does not fare well at all. Throughout the book, with the exception of the chapter on exotic syndromes, one is struck by the relative neglect of the international literature, and this weakness is most evident in this chapter. In the discussion of bizarre delusions no reference is made to the Jasperian criteria of understandability, historically the earliest one. In the discussion of negative symptoms, there are no references to the European work on their definition. In the discussion of schizophreniform disorder, there is no reference to Langfeldt's work (1) or the history and controversy behind the use of the term "schizophreniform" in *DSM-III*. In the presentation of the arguments to rule out an organic cause for schizophrenia there is no reference to the classic review by Davison and Bagley (2). Although it is noted that the diagnosis of acute psychotic episode is commonly used but has never had a place in the official nomenclature (p. 196), Dr. Skodol does not discuss the pros and cons of including such a diagnosis in *DSM*. Similarly, the advantages or disadvantages of deleting acute and chronic subtypes of delusional disorders in *DSM-III-R* are not discussed.

The changes made in *DSM-III-R* in the mood disorders are covered well, with particular attention to subtypes and terminology. Several aspects of the diagnosis of major depression that were confusing in *DSM-III* and that *DSM-III-R* overcame are lucidly presented. These include 1) setting the threshold for clinical significance, 2) the relationship of major depression to other diagnostic concepts of depression, 3) clinical utility of subtypes of depression, and 4) differential diagnosis from other mood disorders and normal grief. In the discussion of anxiety syndromes, Dr. Skodol notes the refinement of criteria for panic disorder, including the requirement of a crescendo pattern. Many subtle and useful distinctions between *DSM-III* and *DSM-III-R* regarding panic and phobic anxiety (pp. 285–286) are highlighted. The discussion of the relation

between panic and depression is good, and the discussion of psychological factors affecting physical illness is excellent (pp. 326–328). In the same chapter there is a simple and clear description of sexual dysfunction disorders.

A critical contribution of this book comes from the chapter on personality disorders. Dr. Skodol comments that the widespread practice of diagnosing a personality disorder after interviewing only the patient (with or without a structured instrument) is basically flawed and that diagnosing personality disorder in the presence of axis I disorders might not be valid. Yet these practices prevail widely. Dr. Skodol points out that it is critical to involve a third-party informant in the evaluation of personality. The main weakness of this chapter is that the discussion of an axis that would deal with defenses is limited, although the topic has aroused much controversy and continues to be heatedly discussed by nosologists.

Dr. Skodol notes that *DSM-III-R* was motivated by the experiences of clinicians in an explosion of research on nosologic issues in psychiatry, which is a surprising statement given that there were only 6 years between the two systems. The book is a good addition to the *DSM* library and very useful to nosologists. With *DSM-IV* on the horizon, however, clinicians might as well wait for the next edition to get the best value for their money.

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SLEEP MEDICINE

Atlas of Sleep Medicine, edited by John W. Shepard, Jr., M.D. Mount Kisco, N.Y., Futura Publishing Co., 1991, 279 pp., \$150.00.

The *Atlas of Sleep Medicine* will serve as a landmark in the standardization of the field. The book provides a variety of photographs of actual polysomnographic recordings from patients with sleep disorders, captioned by several-paragraph explanations of the key features to be recognized in the recordings. Polysomnography serves the sleep disorders clinician in the analysis of sleep complaints in the same manner as the electrocardiogram serves the cardiologist in the analysis of chest pain. Until the publication of this atlas, there has been no standard reference to connect sleep disorders clinicians in different centers in their interpretations of the polysomnographic record.

The atlas is divided into ten sections. Section one, Recording Montage, outlines the individual recordings in a standard polysomnographic report. Section two, Recording Artifacts, outlines signals in the record that are extraneous to the variables of interest. Section three, Normal Sleep, shows recordings of different stages of sleep in adults, neonates, and children. Section four, Snoring and Sleep Disordered Breathing, shows recordings of snoring, hypopnea, cardiac arrhythmias associated with sleep-related breathing events, and central, obstructive, and mixed apnea as well as nasal continuous-

positive-airway-pressure correction of sleep apnea. Section five, Trend Oximetry, displays oximetry profiles showing patterns of oxyhemoglobin desaturations associated with sleep apnea. Section six, Movement Disorders and Parasomnias, shows examples of periodic limb movements, bruxism, REM-sleep behavior disorder, sleepwalking, night terrors, body rocking, and sleep-related panic attacks. Section seven, Epileptiform Abnormalities, shows polysomnographic recordings of epileptic activity during sleep. Section eight, Miscellaneous Polysomnographic Findings and Nocturnal Penile Tumescence, shows examples of such phenomena as hiccups and swallowing as well as examples of nocturnal penile tumescence recordings. Section nine, Daytime Sleepiness: Multiple Sleep Latency Test and Pupillography, shows examples of these recordings used in complaints of hypersomnia. Section ten, Actigraphy, shows recordings of wrist actigraphs used in a variety of clinical indications, such as sleep/wake schedule disorders, to give measures of daily motor activity over longer periods of time (for example, 1 week).

This clinical reference book is the combined effort of a highly competent staff at the Sleep Disorders Center of the Mayo Clinic and Mayo Foundation, Rochester, Minn., including John Shepard, Peter Hauri, and Cameron Harris. In all, 127 high-quality photographic reproductions of actual sleep recordings are displayed. With each is a rich, thoughtful guide to the individual case study, including interpretation of the record and recommendations for clinical management. The wise descriptions of the polysomnographic vignettes draw on the vast experience of the laboratory at the Mayo Sleep Disorders Center. Due to the specificity and technical nature of the atlas, it will be most beneficial to the sleep disorders clinician, although the clinical vignettes provide valuable insights for generalists attempting to understand the sleep complaints of their patients.

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TREATMENT

Psychiatric Treatment: Advances in Outcome Research, edited by Steven M. Mirin, M.D., John T. Gossett, Ph.D., and Mollie C. Grob, M.S.W. Washington, D.C., American Psychiatric Press, 1991, 320 pp., \$25.00.

In 1624, John Donne wrote, "I observe the physician with the same diligence as hee the disease," and our paymasters have adopted this as their current motto. As a profession we physicians can no longer get by with the "because I say so" approach to medical practice. We are highly accountable these days, and our assessments of disease have to be objective, our treatments rational, and our results predictable.

This leaves psychiatry in a very difficult position because our syndrome descriptions and disease classifications are still quite unscientific. When we look at outcome results, not only are we uncertain of what has happened but in fact we are often not sure what it is we just treated. This is a reprehensible situation, particularly when, paradoxically, we continue to accumulate some potent therapies in several modalities.

Many of psychiatry's illnesses have very prolonged courses, and not many psychiatrists have the luxury of pursuing them from beginning to end, as Kraepelin and his contemporaries did. We have very few firm outcome criteria, and, worst of all, so far as statisticians are concerned, psychiatric illnesses do

not have much of a death rate, so it is difficult to give dramatic proof that our interventions save lives. That we are more in the business of saving quality of lives is not a terribly popular point of view to put forward to third-party payers these days.

It is bordering on the trite to say that the huge number of psychiatrically ill individuals in the community causes untold suffering and enormous economic loss. It is equally trite for psychiatry to say that it can do something about this unless we can prove that this is true and, equally importantly, show that our methods are better than anyone else's.

Psychiatric Treatment: Advances in Outcome Research makes a worthy, if somewhat tentative, attempt to break into the totally unsatisfactory situation we have today in outcome research in psychiatry, in which follow-up studies are sparse; measures of diagnosis, treatment, and outcome are idiosyncratic; and confirmatory investigations are rarely done. The editors state up front that the initiative to take a new look at outcome research in psychiatry in the United States is mainly a fiscal one. The managed care industry is making its demands, and psychiatry cannot plead special case status. Therefore, and this is the book's message, we had better learn how to define illness more clearly, treat it more specifically, and measure the outcome of the treatment more meaningfully. Otherwise, the management of our patients may be taken largely out of our hands.

The book is a series of edited essays discussing a fairly wide range of psychiatric disorders and emphasizing treatment outcome. Unfortunately, this field in psychiatry is pathetically meager, and one gets the impression that both editors and writers are scrambling for material. Despite its worthwhile aims, the book too often becomes bogged down in the obvious, and its message, although true, becomes repetitive.

At the present stage of development in psychiatry, the beginning of our treatment is too often geared to a short-term end. We have to begin to look much farther ahead and become aware of the fuller implications of disease outcome, so that our therapeutic plans can be realistically geared to the best-quality treatment and the best possible outcome for the patient. No insurer is going to be impressed if the "cured" patient continues to require frequent readmissions to an institution, and we as clinicians should not be happy with that state of affairs either.

Here in Canada, with our comprehensive medical care system, we tend to be smug about the open-market approach to health care in the United States. However, our system is under as much financial pressure as yours and we are increasingly being held responsible for the efficacy of our treatments and for their longer-term outcome. Because of the particular pressures on the U.S. system, you are becoming leaders in this area of research and practice, but the present volume shows very clearly how amateurish all of us are at present in delineating and measuring outcome factors. It should shame us into taking urgent action.

I have only one quarrel with the book's approach. Throughout, its message is more efficiency and more economy. Nowhere did I find a clear statement that, in the United States as in other developed economies, mental health services have always been desperately underfunded. Many of us are afraid that, in conforming with the need to make the rest of medicine more cost effective, psychiatry will be cut to the bone and beyond. I hope that future advances in outcome research will demonstrate not only our inefficiencies but also the enormous gaps in the services we are allowed to provide.

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Treatment Strategies for Refractory Depression, edited by Steve P. Roose, M.D., and Alexander H. Glassman, M.D. Washington, D.C., American Psychiatric Press, 1990, 160 pp., \$28.00.

Clinicians who turn to the psychiatric literature for help with patients with refractory depression are faced with a complex and diverse assortment of treatment recommendations. Although there is no shortage of advice available, strategies based on well-designed studies using standardized patient selection criteria and rigorously controlled treatment interventions are rare. In fact, most of the literature on which currently touted treatment recommendations for refractory depression are based consists of anecdotal reports and uncontrolled studies involving heterogeneous patient populations. Most studies are also short-term in nature and lack long-term follow-up data. Unfortunately, it also is common practice for clinicians to literally "experiment" on patients with various combinations of psychotropics before the safety and efficacy of such regimens are established. This type of polypharmacy would be considered unacceptable if held to the standards of therapeutic practice for other medical specialties. With the recent introduction of several new psychotropics and the increasing practice of applying "nonpsychiatric" drugs (such as calcium channel blockers) to psychiatric disorders, a concise analytic summary examining the scientific literature on the treatment of refractory depression has been needed. In this regard, this text, superbly edited by Roose and Glassman, is a valuable contribution to the clinical literature.

The reasons for the lack of methodologically rigorous studies of refractory depression are noted in the introductory chapter by Roose. Simply stated, the primary methodologic problem involves recruiting sufficient numbers of diagnostically homogeneous patients for statistical analysis and then rigorously sequencing treatment interventions over time as well as controlling for numerous potential confounding variables (particularly on axis II). After these basic problems, which are intrinsic to most currently available studies of refractory depression, are acknowledged, the remainder of the text coalesces and critically evaluates the treatment literature through late 1988. Topics that are examined include the relationship

between tricyclic serum levels and treatment response, lithium and thyroid augmentation strategies, and use of monoamine oxidase inhibitors. Applications of anticonvulsant medications such as carbamazepine and valproate are also discussed, and most of the emphasis is on bipolar disorder. The germinal literature on calcium channel blocking agents is discussed, but the more recent controlled investigations in this area supersede any dealt with here. The chapter on ECT focuses predominantly on response rates of patients who are resistant to antidepressant medication. A more timely and perhaps more useful focus for the ECT chapter would have been on the relative efficacy of unilateral versus bilateral electrode placement and the significance of charge dosing on treatment response. Clinicians seeking timely advice on these latter issues will also need to consult the more recent literature on ECT. The chapter on chronic depression and the role of axis II disorders in the phenomenon of treatment resistance has a predominantly descriptive and epidemiologic orientation. The contribution of developmental factors—particularly emotional deprivation and psychological trauma—are not examined. The psychotherapeutic and psychosocial management of patients with refractory depression is also not addressed.

These limitations largely derive from the limited scope that is inherent in the framework of the text, which is part of the Concise Guide series of the American Psychiatric Press, compiled from symposia presentations at APA annual meetings. From the standpoint of psychopharmacologic management, however, the text represents an extremely valuable compilation and critical analysis of the literature—at least through 1988—that should be quite useful to clinicians involved in the treatment of patients with refractory mood disorders. From an academic standpoint, the text also raises the standard by which future investigations and claims of therapeutic efficacy for refractory depression will be held. This should help facilitate standardized approaches in the clinical care of this difficult patient population.

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Reprints of Book Forum reviews are not available.

Visual Hallucinations After Combining Fluoxetine and Dextromethorphan

SIR: I would like to report the occurrence of visual hallucinations in a patient treated with fluoxetine when she used a cough syrup containing dextromethorphan. To my knowledge, such interaction has not yet been reported in the literature.

Ms. A, a 32-year-old obese patient with a 20-year history of dysthymia, presented with manifestations of major depression. She complained of sadness and guilt, anhedonia, initial insomnia, and early morning wakening. She also expressed feelings of helplessness and hopelessness. A brief treatment trial with doxepin was terminated because of drowsiness and her fear of gaining more weight. A regimen of fluoxetine, 20 mg/day, was started. On the 17th day of treatment, Ms. A had symptoms of a common cold including congestion, runny nose, and cough. She took two teaspoonfuls of a cough syrup containing dextromethorphan. She had no prior side effects with that drug. The next morning, she took two more teaspoonfuls of the cough syrup with her fluoxetine capsule. Two hours later, she experienced vivid hallucinations of bright colors and distortions of the shapes and dimensions of her surroundings. The hallucinations lasted 6–8 hours, then stopped. They were very similar to her past experience with LSD 12 years earlier. Fluoxetine was discontinued at Ms. A's request. She also refused any other antidepressants. I continued to see her in therapy for another year, with some improvement, and without recurrence of the hallucinations.

Fluoxetine is a specific serotonin (5-HT) reuptake inhibitor (1), and dextromethorphan is an NMDA receptor antagonist related in its site of action to phencyclidine and ketamine (2). However, dextromethorphan does not have any known psychomimetic effects (3). It is known that 5-HT₂ receptors mediate the hallucinogenic effects of LSD (4). Also, there is some suggestion of a functional interaction between glutaminergic and serotonergic pathways (5). An electronic literature search did not produce any reports of visual hallucinations caused by fluoxetine or dextromethorphan. The patient used each of the drugs alone without side effects. The hallucinations appeared only when both drugs were combined. This suggests a synergistic action of the drugs in this patient. "Flashbacks" or "post hallucinogen perception reaction" may be another explanation. However, the long duration of the hallucinations (6–8 hours) makes this conclusion unlikely.

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Acute Exacerbation of Body Dysmorphic Disorder During Tryptophan Depletion

SIR: Recent literature has examined the relationship between body dysmorphic disorder and obsessive-compulsive disorder (1, 2). Serotonin reuptake inhibitors have been reported to be effective in treating both conditions (3). We report effects of acute tryptophan depletion in a patient with a history of major depression and obsessive-compulsive disorder who met *DSM-III-R* criteria for body dysmorphic disorder. The patient participated in an ongoing study of the effects of acute tryptophan depletion on mood and obsessive-compulsive symptoms in patients with obsessive-compulsive disorder treated with 5-HT reuptake inhibitors.

Ms. A was a 42-year-old woman with a past history of major depression responsive to treatment with monoamine oxidase inhibitors (MAOIs). Most prominent throughout her course however, and unresolved with MAOI treatment, were obsessive concerns about her face and appearance, which fulfilled criteria for body dysmorphic disorder. Picking and filing at perceived facial imperfections consumed hours at a time, leading to wounds and secondary infections. Five years prior to the study reported here she developed counting rituals and compulsions involving symmetry and exactness, which prompted the additional diagnosis of obsessive-compulsive disorder. Treatment with clomipramine, 200 mg/day, and buspirone, 60 mg/day, was associated with near elimination of picking and filing, leading to healing of her face and a normal appearance at the time of examination. The patient did continue to spend up to an hour a day examining her face and obsessing about its imperfections. Her other obsessive-compulsive symptoms resolved completely.

Compared with sham depletion under double-blind conditions, acute tryptophan depletion produced a dramatic exacerbation in her dysmorphophobia. She became afraid that people were looking at her face, turned away from the open door of the testing room, and made repeated trips to the bathroom to stare in the mirror. The patient also became extremely tearful, reporting, "I don't know why I am crying all the time. I don't have anything in particular to

feel sad about." Sham depletion produced only very mild nausea, without change in the patient's affective state or level of concern regarding her face.

Administration of a low tryptophan diet coupled with an amino acid drink devoid of tryptophan has proven a safe and reliable method for producing lowered plasma tryptophan levels (4). Delgado et al. (4) have demonstrated the reemergence of depressive symptoms in depressed patients treated with 5-HT reuptake inhibitors when plasma tryptophan levels are acutely lowered in this manner. This effect is presumably mediated through a reduction in brain 5-HT, as decreases in plasma tryptophan have been shown to reduce brain 5-HT in preclinical studies (5).

The exacerbation of both depression and body dysmorphic disorder associated with acute tryptophan depletion suggests that 5-HT reuptake inhibitors used in the treatment of these syndromes share a common mechanism of action that depends upon the ongoing availability of 5-HT. That Ms. A's obsessive-compulsive symptoms were not exacerbated by tryptophan depletion is consistent with other preliminary results of tryptophan depletion in patients with obsessive-compulsive disorder treated with 5-HT reuptake inhibitors (Barr et al., unpublished data).

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Effect of Estrogens on Thyroid Function

SIR: Estrogens are thought to exert rather minor actions upon intrinsic thyroid function, yet the literature concerning the effects of estrogens on thyroid function has provided conflicting results (1, 2). Oral estrogens are known to increase synthesis of thyroid binding globulin with a consequent rise in T_4 and T_3 , yet plasma concentrations of free T_4 and T_3 remain unchanged. Frank hyperthyroidism has not been described in association with estrogen use, yet the following is a case in which some symptoms typical of hyperthyroidism resolved after discontinuation of oral estrogens, corresponding with normalization in thyroid function tests.

Ms. A, a 21-year-old woman, presented with a chief complaint of, "I just can't stop crying." She had an 8-month history of crying episodes that had increased in frequency and duration, making her unable to work or interact with those outside her family. Psychosocial stressors were minimal; she denied feelings of sadness and neurovegetative

symptoms. On presentation, her only physical finding was sinus tachycardia (120 bpm); her only medication was ethinylestradiol 0.05 mg/norethindrone 1 mg, which she had been taking regularly for 1 year on a 28-day cycle.

Laboratory results were normal except for the following thyroid function tests: thyroid-stimulating hormone (TSH)=1.4 μ U/ml (normal=0.5-4.5 μ U/ml); T_4 =17.4 μ g/dl (5.5-11.8 μ g/dl); T_3 uptake=31.2% (35.9%-43.5%); and free T_4 index (FTI)=5.4 (2.3-5.23). Estrogen was discontinued, and 2 weeks later, thyroid function tests were largely unchanged (T_4 was 14.8 μ g/dl). There was little improvement in symptoms. Four weeks after discontinuation, crying spells were reduced by 50% (1-3 per 2 days), pulse was 100 bpm, and thyroid function tests were as follows: TSH=1.9 μ U/ml, T_4 =13.1 μ g/dl, T_3 uptake=32.9%, and FTI=4.31. Finally, 2 months after discontinuation, Ms. A was free of crying spells, thyroid function tests were normal (TSH=1.3 μ U/ml, T_4 =11.8 μ g/dl, T_3 uptake=36.6%, and FTI=4.25), pulse was 82 bpm, and she was completely functional.

Mood changes associated with oral contraceptive use are well documented; 60% of oral contraceptive users report some degree of affective symptoms, and 10% will discontinue their use due to depression or irritability (3). Our patient had a marked elevation in T_4 on presentation, atypical for estrogen use, and symptoms resolved as thyroid function tests normalized in the absence of exogenous estrogen. This is the first reported case that entertains the possibility of estrogens affecting behavior through alterations in thyroid function. Estrogens have been demonstrated to alter levels of TSH in vivo (2). However, evidence that the thyroid function test results may have been incidental is provided by Cohen's study in which 18% of adult psychiatric inpatients had abnormal thyroid function, and about 50% of these patients had a spontaneous normalization of values in 2 weeks (4).

Although direct cause of symptoms is not unequivocal, this case serves to expand the data regarding endocrine-associated psychiatric symptoms and aids the clinician in treating patients with psychiatric complaints who are using oral contraceptives.

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Bupropion-Induced Carbohydrate Craving and Weight Gain

SIR: This letter reports the case of a 44-year-old man with a 12-year history of chronic pain and accompanying major depression of relatively recent onset.

Mr. A was seen in an outpatient pain clinic and found to suffer from recurrent major depression of approximately 4-month duration. The patient, in addition to displaying

several typical features of depression, also exhibited several "atypical" symptoms, including excessive eating, particularly when under stress (baseline weight=195 lb), prominent anxiety, and rejection sensitivity.

Mr. A developed severe urinary hesitancy after titration of doxepin to 100 mg h.s. This resolved during a 10-day washout period, and the patient was then started on a regimen of desipramine. After titration to 50 mg b.i.d., the patient developed severe urinary retention necessitating discontinuation of desipramine and treatment with bethanechol. Mr. A remained seriously depressed, with an essentially unchanged Hamilton Rating Scale for Depression score of 24 and a Symptom Questionnaire Depression T score of 90 (1).

After a 2-week washout period, the patient was started on bupropion at a dose of 100 mg b.i.d. for 3 days, increasing to 100 mg t.i.d. No side effects were noted at 2 weeks, and the patient reported much improvement in mood, sleep, energy level, and even anxiety symptoms. Mr. A also reported decreased sensitivity to criticism from others. At week 4, he had a Hamilton depression scale score of 12 and a Symptom Questionnaire Depression T score of 60. However, the patient exhibited a 12-lb weight gain and reported carbohydrate craving, particularly at night. Mr. A was so pleased with his overall response that he felt he could tolerate this modest weight gain. At 8-week follow-up, however, the patient exhibited a 31-lb weight gain from baseline and was quite disturbed at his continued carbohydrate craving, describing himself as "living in front of the refrigerator at night." Although the patient had maintained the improvements already cited, at his insistence, he was tapered off of bupropion over a 10-day period and treated with cognitive behavior therapy only. At a 1-month follow-up, the patient reported a return to his baseline appetite and exhibited a weight which was 15 lb over his baseline. He continued to deny significant symptoms of depression with a Hamilton depression scale score of 8. At a 2-month follow-up, his weight was only 6 lb over baseline, and his Hamilton depression scale score was 6.

Although the 1992 edition of *Physicians' Desk Reference* reports weight gain in 9.4% of patients treated with bupropion, as compared to 34.5% of patients treated with tricyclics, several major references in clinical psychopharmacology suggest that significant weight gain with bupropion treatment is rare (2, 3). Further, there is no reference to carbohydrate craving with bupropion in any of the major literature sources. Whether the severe weight gain and carbohydrate craving during treatment with bupropion was due to our patient's subtype of depressive illness (Mr. A exhibited a combination of both typical and atypical symptoms) is a question that requires research on the differential pharmacological response across depression subtypes. Also, further research into the mechanism of action of bupropion may help explain our observations.

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Possible Clozapine Exacerbation of Bulimia Nervosa

SIR: Clozapine is a new antipsychotic agent reported to induce significant weight gain (1, 2). We report a case of a patient with bulimia nervosa and schizoaffective disorder whose bulimia became acutely worse after switching from thiothixene to clozapine.

Ms. A was a 29-year-old woman with a long history of bulimia nervosa that was followed by the development of a schizophrenic illness characterized by paranoid delusions, auditory hallucinations, and major affective symptoms. She was treated initially with thiothixene with a good response. Her bulimia and psychosis eventually stabilized on thiothixene, 10 mg h.s., and fluoxetine, 80 mg every morning.

After several months on this regimen, during which time Ms. A attended college, was nonpsychotic, and generally abstinent from binge eating and purging, she developed the initial signs of tardive dyskinesia. She was then switched to clozapine (up to 350 mg/day), which worked well for her psychosis with fewer side effects. During initiation of clozapine therapy she experienced no major psychosocial stressors and was maintained on fluoxetine, 80 mg/day. Ms. A began binge eating and purging approximately 6 weeks after beginning clozapine treatment, with as many as four binge-purge episodes per day. Before this time she had been completely abstinent for several weeks. The relapse of this patient's eating disorder continued for several months, did not respond to supportive and cognitive-behavioral techniques, and eventually required hospitalization. The patient gained over 17 pounds; however, her tardive dyskinesia was almost completely resolved 8 months after discontinuing thiothixene.

Although we did not switch back to thiothixene and rechallenge with clozapine, it is our clinical impression that the acute and marked changes following clozapine initiation strongly suggest an association. A resubstitution of thiothixene might more clearly establish this association, but we did not consider this to be ethical or clinically indicated. Although clozapine certainly offers great advantages over typical antipsychotic medications, we feel that the use of clozapine in the treatment of psychotic patients with a history of bulimia nervosa must be approached with caution, as vomiting can be life threatening. The subsequent electrolyte disturbances following vomiting may further predispose patients to seizures induced by clozapine. Since clozapine blocks serotonergic transmission, it may be that the exacerbation of this patient's bulimia involved compromise of serotonin function despite treatment with fluoxetine (3, 4). The development of tolerance to fluoxetine may be a possibility, but has not been reported to occur with bulimia.

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No Gender Effect on Age at Onset in Familial Schizophrenia?

SIR: In the last decade, gender differences in schizophrenia renewed interest in the understanding of the heterogeneity of the disease. One of the most consistently reported gender differences in schizophrenia is the earlier age at onset observed in men (from 18 to 25 years) compared to women (from 25 to 35 years) (1). Although, Loyd et al. (2) found no gender effect for developing schizophrenia among the psychotic relatives of schizophrenic patients, Pulver et al. (3) reported a higher risk of developing schizophrenia in relatives of early onset male subjects and no association between age at onset and risk for schizophrenia among the relatives of female subjects. However, a large body of literature shows that the early onset syndrome in males with negative symptomatology and chronic evolution is characterized by an absence or a very low frequency of familial psychosis.

While identifying multiply-affected families for the purpose of linkage analysis, we surprisingly found no gender effect for age at onset of schizophrenia. A sample of 104 schizophrenic patients (70 men and 34 women), meeting *DSM-III-R* criteria and belonging to families containing at least one affected first-degree relative (sibling and/or parent), was identified in two French metropolitan and rural settings. All probands and relatives were interviewed with the Schedule for Affective Disorders and Schizophrenia—Lifetime Version Modified for the Study of Anxiety Disorders (SADS-LA). Age at onset was defined as age at first hospitalization, since this date is highly correlated with the beginning of acute symptoms and represents an exact measurement (4).

No difference was found between the mean age at onset among schizophrenic men (mean=24.0 years, SD=6.5) and women (mean=24.9 years, SD=7.2). This striking absence of difference in age at onset remained present at all age periods: 73% of men versus 63% of women had an age at onset between 26 and 35 years; and 6% versus 10% had an age at onset of 36 years or older.

The reported absence of a relationship between age at onset and sex cannot be attributed to an eventual cultural effect, since no statistical difference emerged when comparing the age at onset of the two subsamples of metropolitan (mean=23 years, SD=4.4) and rural patients (mean=25.1 years, SD=7.7). One should also point out that the age of onset of schizophrenia is not necessarily synonymous with first hospitalization. Thus, women could nonetheless have a later age at onset, while those hospitalized early could belong to a subgroup not tolerated any longer at home.

Still, our results could suggest that among multiply-affected families, schizophrenic men have a somewhat later onset than that usually reported in the literature. This supports the hypothesis that early onset syndrome in males is characterized by an absence of familial psychosis. This absence of gender effect for age at onset in multiply-affected families with schizophrenia should nevertheless be replicated in other populations of familial schizophrenic patients.

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Gender Differences in Comorbid Anxiety and Mood Disorders

SIR: We recently analyzed diagnoses based on the Structured Clinical Interview for DSM-III-R (SCID) for a large consecutive series of patients seen at our Center for Cognitive Therapy. We believe our findings are somewhat unexpected. In particular, we found that the ratio of women to men is approximately 1:1 for anxiety or mood disorders for which there was no secondary axis I diagnosis, but approximately 2:1 for a comorbid disorder in which an anxiety or mood disorder was either the first or second diagnosis. In our series of 1,051 patients, we found these rates of primary and secondary mood and anxiety disorders for men and women, respectively: 14.4% and 15.5% for mood disorders only; 7.0% and 9.1% for anxiety disorders only; 10.2% and 19.5% for primary mood disorder plus secondary anxiety disorder; and 9.3% and 14.9% for primary anxiety disorder plus secondary mood disorder ($\chi^2=13.69$, $df=3$, $p<0.01$).

Our findings for the pure mood category stand in contrast to the usual reports (1-4) of mood disorders predominating in women, whereas our findings for the mixed anxiety-mood category are consistent with these prior reports. To our knowledge, prior studies of gender differences in mood disorders have not taken into account whether or not there is a coexisting anxiety disorder.

Our analyses suggest that there is a strong gender component to the mixed anxiety-mood concept. This may be of interest to investigators working to define a *DSM-IV* disorder around this concept.

We are interested in knowing whether other investigators have noted this gender difference.

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Panic Disorder in Benin, West Africa

SIR: Studies of panic disorder among black Africans are very rare. We wish to report 32 cases of panic disorder diagnosed according to *DSM-III-R* criteria after a nonstructured clinical interview. The cases were systematically collected among 351 Beninese patients, whom I personally examined and followed during a 14-month period.

Nor only does panic disorder appear not to be rare in this population (prevalence rate in our patient population=9.1%), it presents many similarities to Western descriptions (1, 2). Although women were not overrepresented in the panic disorder group (17 women versus 15 men), the total patient population included more men than women (205 versus 146). Panic disorder patients were young; mean age at onset was 28 years (SD=9). Half of them (53%) had at least one attack per day with a mean duration of 39 minutes (SD=30). There was a great similarity in clinical aspect: the mean number of symptoms among the 13 symptoms from the *DSM-III-R* list was 7.1 (SD=2.0), with no symptom having a frequency lower than 30%. The two most frequent symptoms were the same as reported in Western studies: palpitations or tachycardia (81%) and dizziness (78%). Cognitive symptoms were not usually volunteered, but rather presented in the guise of somatic complaints (e.g., "heat in the head," a classic African expression of psychic distress [3]). However, upon inquiry it appeared that the Beninese patients experienced the same cognitive symptoms as Western patients: fear of dying (69%), fear of going crazy or doing something uncontrolled (31%). Cultural interpretation was sometimes needed. For instance, fear of going crazy could be expressed in this way: "During the attack, I could see myself walking naked in the streets." In black Africa only chronically mentally ill people walk naked in the streets. In a few cases patients developed persecutive concern about bewitchment, as is common in depressive African patients.

Comorbidity occurred with the same disorders as in Western countries (1, 2): agoraphobia (44%) and generalized anxiety (41%). Both agoraphobia and generalized anxiety were associated in 28% of the patients with panic disorder. Phobic reaction was provoked by going out in the street or to public places for 10 of the 14 agoraphobic patients. Sixty-nine percent of the patients with panic disorder had associated depressive symptoms, reaching the level of major depression (using slightly modified *DSM-III-R* criteria [4]) for 47% of that group.

Our data confirm that there seems to be little evidence available to suggest that panic disorders are fundamentally different in black Africa, either in prevalence or in form.

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The Serotonin Syndrome

SIR: In addition to the description of the serotonin syndrome by Sternbach (1), we would like to report a very severe syndrome following the administration of the serotonergic tricyclic antidepressant clomipramine.

Mr. A, a 30-year-old man with no medical history, had been recently hospitalized for major depression. He was suffering from recurrent major depression according to *DSM-III-R* criteria. Two previous depressive episodes, in 1987 and 1989, had been treated with maprotiline (75 mg/day) for the first episode and amineptine (150 mg/day) for the second. Neither of these two antidepressants induced somatic or psychotic complications. Upon the most recent admission, clinical examination was normal. Blood cell count, ionogram, hepatic biological parameters, calcium, and EEG were all within normal limits. The patient had been treated with clomipramine only, given orally. After the first administration of clomipramine (75 mg), he suffered from tremor, diaphoresis, and nausea. Eight days later, Mr. A was still receiving clomipramine, 100 mg/day. Tremor and diaphoresis persisted, and shivering and occasional myoclonic jerks (two or three per hour) of the limbs appeared. One day later, Mr. A became hypomanic, euphoric, ludic, and insomniac. No delirium was observed. His temperature increased slightly from 36.9 to 37.3 °C. Myoclonus became generalized. The patient complained of incessant, diffuse myoclonic activity involving mainly the face, the upper limbs, and the abdominal and chest muscles. Myoclonic contractions of the diaphragm and of the accessory respiratory muscles interrupted normal breathing. The patient was pale, with periorbital cyanosis and abundant sweating. The EEG was highly abnormal without ground rhythms. The main activity was in the delta range and included slow waves, or spikes and waves, or poly spikes and waves. Some of these paroxysmic features were synchronous with myoclonus jerks of the thoracic or abdominal muscles. The contrast CT scan of the brain was normal. The patient's clomipramine level was 0.3 g/liter (therapeutic range 0.5-1.0 g/liter). Clomipramine was stopped and Mr. A was transferred to an intensive care unit. After the concomitant administration of clonazepam (1 mg) and piracetam (1 g), myoclonus disappeared within 1 hour. Mr. A's mother told us that she had suffered, 5 years earlier, from mild myoclonus of the upper limbs after the administration of maprotiline, 75 mg/day, plus clomipramine, 20 mg/day.

This case appears to be rather exceptional for two reasons: 1) the only two published cases (2) of serotonin syndrome induced by clomipramine were observed in patients previously treated with clogyline, an MAO-A inhibitor; and 2) the myo-

clonus was especially severe. Meanwhile, Mr. A fulfilled eight of the 10 diagnostic criteria of the serotonin syndrome (1). Sternbach stressed that no predictive factors of serotonin syndrome are known. We would suggest that the existence, in the family, of a previous antidepressant-induced myoclonus could be a risk factor.

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Interpretation of Language in Diagnostic Criteria

SIR: According to our survey of 30 professionals, there is a pronounced disparity in interpretations of the language in the "Diagnostic Criteria for Major Depressive Episode" in the *DSM-III-R*. This is of particular concern because those criteria are necessary for a number of diagnoses.

The first sentence of the "Diagnostic Criteria for Major Depressive Episode" (*DSM-III-R*, p. 222) is our focus: "At least five of the following symptoms have been present during the same two-week period and represent a change from previous functioning." In our survey, about two-thirds of the respondents interpreted this to mean that each of five symptoms must represent a change from previous functioning, while about one-third assumed that only one symptom needed to change as long as there are a total of five symptoms present during a 2-week period. We address the linguistic interpretation of the "Diagnostic Criteria," as well as a further convolution in the application of those criteria.

The sentence in question is a compound sentence. "At least five of the following symptoms" is the subject of the second clause, "represent a change from previous functioning." It is clear that the correct linguistic interpretation indicates that each of five symptoms must represent a change from previous functioning. This means that if four symptoms were present, say for 3 years, and some event caused a fifth to emerge, there still would not be a major depressive episode. However, we presented such a scenario in our survey, and respondents who had previously said that "a total of five symptoms must represent a change" were split in their assessment of whether a major depressive episode existed. Similarly, the respondents who said that "at least one of the five must represent a change" were also inconsistent in their assessments. In fact, the *DSM-III-R* implies that only one symptom must change by virtue of its assertion that "people with Dysthymia frequently have a superimposed Major Depression." Given that assertion, closer examination reveals that the similarity in the criteria between the two diagnoses makes it entirely unlikely, if not impossible, that all five criteria must change. In other words, there is a contradiction between the language, or the criteria, for major depression and the assertion of the existence and frequency of double depression. Also note other ambiguities; for example the word "previous" insufficiently specifies time with respect to a criteria like "feelings of worthlessness." While the *DSM-III-R* does state that "boundaries of Dysthy-

mia and Major Depression are unclear," there is no need for unclear language in the description of the diagnostic criteria involved in so many diagnoses.

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Panic Disorder and Suicidal Ideation

SIR: Aaron T. Beck, M.D., and colleagues (1) recently reported that outpatients in the Center for Cognitive Therapy with a current diagnosis of panic disorder seldom report suicide attempts on a lifetime basis. The authors concluded that data from the National Institute of Mental Health (NIMH) Epidemiologic Catchment Area (ECA) study demonstrating an association between panic disorder and suicide attempts (2) were "anomalous, warranting further exploration."

1. *Replication of Findings Not Cited by Dr. Beck and colleagues.* Noyes (3) has recently published a comprehensive review of the literature on anxiety, panic disorder, and suicide. Included in his review were 16 follow-up studies, including his own 7-year follow-up study of 81 patients with panic disorder, which found that five patients had made serious suicide attempts, and three had died by suicide over the 7 years. Based on this review, Noyes concluded that the "data indicate that the risk of suicide in panic disorder is substantial."

Lepine et al., (4) drawing from an anxiety clinic in France, have reported that 42% of 100 consecutive patients with panic had attempted suicide (lifetime). Allgulander and Lavori recently reported on 3,302 inpatients with ICD-8-R "pure" anxiety in Sweden and confirmed an association with suicide (3).

Dr. Beck and colleagues point to a report from the ECA (5) on suicidal behavior that did not report panic disorder as a risk factor. A subset of these same ECA investigators have subsequently reanalyzed the ECA data (6) and concluded that we (2) were correct in our conclusion that panic disorder is related to suicide attempts.

2. *Comorbidity.* Dr. Beck and colleagues report on 151 panic patients. Did none of these have secondary depression, which might lead to suicide attempts? Did none of the 485 "mood disorders" patients have prior (or secondary) panic disorder or panic attacks? Results from Fawcett et al. (7) would suggest that the latter should be at increased risk for suicidal behavior. How were "primary" versus "secondary" diagnoses established if current diagnoses were used? Since Dr. Beck and associates only presented current diagnoses, it is not possible to answer these questions.

3. *Who is Referred to the Center for Cognitive Therapy?* The lifetime rate of suicide attempts even in the "mood disorders" group was only 7% in the data presented by Dr. Beck and colleagues. This is a lower rate than would be expected in a clinical sample of depressed patients. Thus, patients coming to the Center for Cognitive Therapy may be a filtered group of psychiatric patients. It is possible that the filtering takes place in the referring source rather than among Dr. Beck's staff. With all due respect to Dr. Beck's fine research on hopelessness and on cognitive therapy, it is still quite possible that patients with a history of suicide attempts are less likely to be referred to a center for cognitive therapy, especially if they have comorbid diagnoses. For example, 49% of 954 depressed patients coming to treatment at six university cen-

ters as part of the NIMH Collaborative Study of the Psychobiology of Depression gave a history of suicide attempts.

Discrepancies in rates of attempts across clinical samples have more to say about differences in clinical protocol screening and local referral practices or "self-selection" into specific treatments than they do about the true rate of suicide attempts in persons with mood or panic disorders in the community.

We conclude that the findings are not anomalous and certainly warrant further exploration on their nature and cause.

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SIR: Dr. Beck and associates reported on the lack of association between panic disorder and suicidal ideation and behavior in clinical populations, in contrast with previous research evidence mainly based on epidemiological studies (1). We investigated the occurrence of suicidal ideations and attempts in a consecutive series of 70 outpatients referred to our Affective Disorders Program (48 women and 22 men; mean age=34.2 years, SD=9.5 years), five of whom satisfied the *DSM-III-R* criteria for panic disorder with agoraphobia. Patients with concurrent major depressive disorder were excluded. Suicidal tendencies were evaluated by the 7-point scale of Paykel's Clinical Interview for Depression, a semistructured research interview (2). This scale consists of specific anchor points, from "no suicidal ideations" (score 1) through "patient has thoughts of taking his life, but would not, and has no plans" (score 4) to "suicidal attempt of any but most minor kind" (score 7). The cut-off point of 4 was found to apply to 75% of patients with *DSM-III* melancholia and to 5% of healthy control subjects (3). Only one of the 70 patients with panic disorder and agoraphobia (1.4%) reported suicidal tendencies, as identified, in the previous month. These findings thus support those by Dr. Beck and colleagues.

Dr. Beck and colleagues discuss several potential explanations for the discrepancies between their clinical study and epidemiological findings (1). We agree that undetected or previous history of mood disorders may be particularly important regarding suicidal behavior. We have data, however, to suggest another explanation of suicidal ideations. Fear of dying is a rather common symptom during panic attacks. In some cases, it may occur also at other times and reach the

intensity of thanatophobia, the unfounded conviction of dying associated with fear of news that provokes thoughts of death (4). Thanatophobia, as measured by Kellner's Illness Attitude Scales, was found to be significantly higher in patients with agoraphobia associated with panic attacks, compared to healthy control subjects, and to wane when agoraphobia was treated by behavioral methods (5). Thirty-eight patients (54.3%) of the 70 here reported scored 4 or above for thanatophobia on the phobia item of the Clinical Interview for Depression. It is rather common in various research interviews to start exploring suicidal ideations by asking whether there has been a period when the patient thought a lot about death. The majority of patients with panic disorder and agoraphobia were found to be obsessed by the idea of death, and yet these thoughts are part of hypochondriacal concerns (4). Unlike experienced clinicians, lay interviewers in epidemiological studies may be misled by these thoughts and interpret them as part of suicidal tendencies.

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Dr. Beck and Colleagues Reply

SIR: Although our article was published in September 1991, we wrote it shortly after reading Dr. Weissman and associates' 1989 article (1). Therefore, we are indebted to them for describing more recent reviews and studies. We concur that the original findings can no longer be considered "anomalous." We address their points below.

1. *Replication.* A critical review of the literature is beyond the scope of this letter. However, many of the studies cited by Dr. Weissman and colleagues are not so supportive as suggested. For example, the 16 studies reviewed in the article by Noyes consist of eight retrospective studies of the relation of *neuroses* (not panic disorder) to suicide attempts and eight retrospective studies of the relation of *anxiety states* or *anxiety neuroses* to suicide attempts. Several of these samples included patients whose diagnoses antedated by several decades the inclusion of panic disorder as a separate entity in *DSM-III*. Also included in this review were six studies of completed suicides, none of which showed a relationship between panic disorder and suicide.

2. *Comorbidity and Multiple Diagnoses.* To test the issues about comorbidity raised by Dr. Weissman and associates, we identified a sample of 559 (31.2%) of 1,794 outpatients consecutively evaluated according to *DSM-III-R* criteria at the Cen-

ter for Cognitive Therapy between 1986 and August 1991 who represented the types of diagnostic combinations that Dr. Weissman and colleagues suggested might be evaluated with respect to past suicide attempts. We excluded patients from 1985 because some of them were diagnosed according to *DSM-III* criteria. All of the current patients were diagnosed with the SCID, and the information about a past suicide attempt was gathered with the Scale for Suicide Ideation as in our previous study. Instead of focusing on just secondary comorbid diagnoses, we extended our scope to tertiary diagnoses.

None of the 53 patients diagnosed with a primary panic disorder for whom there was no comorbidity described a past suicide attempt. Five (3.6%) of the 140 patients diagnosed with a primary panic disorder and either a secondary or tertiary mood disorder described a past suicide attempt. Twenty (6.4%) of the 310 patients diagnosed with a primary mood disorder for whom there was no comorbidity described having made a past suicide attempt, while four (7.1%) of the 56 patients diagnosed with a primary mood disorder and either a secondary or tertiary panic disorder described having made a past suicide attempt. In summary, the presence of a mood disorder, whether primary, secondary, or tertiary, was the consistent correlate of previous suicide attempts.

3. *Referrals to the Center for Cognitive Therapy.* Our finding of 7% for lifetime suicide attempts may not be low for an outpatient sample. In the study by Fawcett (cited by Dr. Weissman and colleagues), 80% of the sample consisted of inpatients, many of whom presumably had been hospitalized because of recent suicide attempts.

A major question is the ascertainment of suicide attempts. Many individuals report having made "suicide attempts" but acknowledge not having had any wish to die. It is possible that our stringent criteria for ascertainment of lifetime suicidal attempts may account for what appears to be a low rate. In any event, there is no discernible basis for the suggestion that patients referred to our clinic were screened out for previous suicide attempts. Regarding the "filtering hypothesis," we have determined that our entire sample of patients has a substantial degree of suicidality. In fact, 587 (32.7%) of 1,794 patients in all diagnostic categories presented with current suicidal ideation.

We recommend that further research, particularly prospective studies, should address a number of methodological, clinical, and conceptual issues before we can arrive at any definitive conclusions. Our recommendations include the following:

1. *Ascertainment of suicide attempts.* A more refined definition that restricts "suicide attempts" to instances in which there is an intent to die and classifies other acts as "deliberate self-harm" or "parasuicide" is suggested.
2. *Definition of panic disorder.* The policy of equating diagnoses of "anxiety states" with the diagnosis of "panic disorder" appears to be unjustified.
3. *Sequence.* Some kind of program needs to be laid out to address the questions of sequence and of proximal versus distal relationships of clinical diagnoses and suicidal attempt.
4. *Comorbidity.* Data should include all of the clinical conditions that can be associated with suicide attempts: affective disorders, multiple diagnoses, depression-anxiety combination, personality disorders (especially borderline personality disorder), and substance use disorders.
5. *Comprehensive study of hypotheses.* Convergent validity of the hypothesized association between panic and suicide should be established on the basis of a variety of related studies: a) community surveys (as in the studies by Dr. Weissman and colleagues), b) clinical examination

of recent suicide attempters, c) examination of individuals currently diagnosed as having panic disorder, d) "psychological autopsies" of completed suicides, and e) longitudinal prospective studies of panic disorder and affective disorder patients.

We appreciate seeing the letter from Dr. Fava and associates who point out several possible sources of error (fear of death, hypochondriacal fixations, etc.) in categorizing death-related thoughts as suicidal ideation. Their overall finding that suicidal ideation is not specifically associated with panic disorder raises further questions regarding the issue of panic disorder as a risk factor in suicidal behavior.

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Seizure With Low Doses of Clozapine

SIR: I refer to a letter to the Editor by Pierre Thomas, M.D., and Michel Goudemand, M.D. (1). From the letter it appears that the patient in reference was prescribed clozapine after he did not respond to treatment with haloperidol, 20 mg/day. If this is so, by current standards prevalent in the United States, the use of clozapine would have been premature.

Use of a medication with the potential for complications that is carried by clozapine should be reserved for cases where alternative treatments have been reasonably exhausted. While most patients would respond to haloperidol, 20 mg/day, some patients may require higher doses, and if that failed, a trial with another "conventional" neuroleptic would have been in order. I hope that the letter of Drs. Thomas and Goudemand will serve to encourage us to maintain these standards.

REFERENCE

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JOSEPH MORE, M.D.
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Dr. Goudemand and Dr. Thomas Reply

SIR: We agree with Dr. More's advice about the reserves and precautions to be taken before implementation of clozapine treatment.

However, our purpose was to mention an unusual adverse effect (seizure with low doses of clozapine) and consequent particular precautions (i.e., during EEG) to be taken while increasing dosage. Thus, we did not go deeper into the reasons why our patient was prescribed clozapine treatment. With haloperidol treatment, psychotic features and delusions persisted unchanged, moreover, our patient experienced incapacitating and incorrigible extrapyramidal symptoms. In our clinical experience such a combination required an increase in dosage, as well as the use of another "conventional" neuroleptic.

In our ward, since 1989 only 10 patients have been pre-

scribed clozapine among about 150 patients admitted for schizophrenic disorders each year. We hope this ratio testifies to our respect of the "standard" in prescribing clozapine.

The choice of a treatment is made after careful consideration of a patient's individual situation and after weighing benefits and disadvantages. Exclusive and uniform "standards" may damage quality of clinical practice.

MICHEL GOUEMAND, M.D.
PIERRE THOMAS, M.D.
Lille, France

Psychiatric Consultation-Liaison Intervention and Hospital Stay

SIR: I read with much interest the article by James J. Strain, M.D., and colleagues (1) examining the effect of a psychiatric consultation-liaison intervention on length of hospital stay and disposition status of elderly patients with hip fractures. The authors concluded that admission psychiatric liaison screening of these elderly patients resulted in early detection of psychiatric morbidity, better psychiatric care, earlier hospital discharge, and substantial cost savings to the hospital. However, the design of their study raises questions as to the specificity of the effect of psychiatric screening on reducing length of stay and thus the cost savings generated.

The design of their study, comparing the outcomes mentioned above among patients in an orthopedic unit between a nonintervention (or "control") year and a subsequent psychiatric intervention year, has its limitations. Perhaps the greatest weakness of this design is that it is not possible to be sure that the reduction in length of stay observed during the intervention year was due to the specific effect of psychiatric screening rather than nonspecific factors such as the effect of observation on the orthopedic unit's practices. Unfortunately, it is not clear whether the authors incorporated an appropriate experimental condition during the nonintervention year that would control for such nonspecific effects of observation, thus weakening the evidence for their conclusions. Furthermore, demographic (age, gender, marital status, socioeconomic class) and clinical (premorbid level of function) variables that could affect length of stay may have differed between the control and intervention years. However, data were not presented showing comparability of intervention and control years with respect to these factors, again weakening the inferences that can be made about the impact of psychiatric intervention.

While designing a study to address these methodological issues may be difficult, if not impossible, one way of obtaining indirect evidence for the specific effect of psychiatric intervention in reducing length of stay would be the demonstration that the reduction in length of stay seen in the intervention year was confined to patients with, rather than without, psychiatric comorbidity. Further, it would be reassuring to know that patients with psychiatric comorbidity in the intervention year had a shorter length of stay than patients with equivalent comorbidity in the control year.

Despite these criticisms, I congratulate the authors on attempting an important study in such a methodologically complex area. Perhaps the limitations of their method might have warranted some discussion in their article.

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PHILIP MORRIS, M.D., PH.D.
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SIR: We read with great interest the recent paper by Dr. Strain and colleagues. However, we question the authors' basis for their conclusions.

The early detection claim seems self-evident, but it is unclear if the *DSM-III-R* diagnoses presented were made just at admission or at any time during the hospitalization. It is not unusual to find delirium appearing several days after surgery (1). Delirium should be separated from dementia since the interventions and prognoses are quite different and the latter is often known prior to admission and does not require a psychiatric consultation to detect it "early" in the hospitalization. With respect to depression, were any of the patients prior to admission taking antidepressants that could cause orthostatic hypotension and lead to falls and fractures?

The claim of "better psychiatric care" is hard to evaluate without any data on what psychiatric care was provided. At Mount Sinai patients were only seen for 2.4 visits on average. Were medications added or stopped? Was psychotherapy provided to patients or families? Was the diagnosis used to improve discharge planning?

The claim of "earlier discharge" is impossible to evaluate since the data from the intervention year were compared to a baseline year without any evidence that the populations were identical or that nothing had changed in terms of pressures on length of stay.

The claim of "substantial cost savings" rests on unspecified assumptions as to how the hospitals are reimbursed or could reduce expenses. It is unclear what the full cost (direct and indirect) is of the psychiatrist's time for the liaison and consultation activities. Is the \$80/visit the charge or payment? For what kinds of visits? Why didn't "better psychiatric care" lead to any cost savings from more patients going home rather than to expensive nursing homes? Change scores at discharge for the Geriatric Depression Scale and the Mini-Mental State exam should be calculated for individual patients in relation to their own scores at admission and not in comparison to a different group of patients in the baseline year.

Some of the above analyses may be possible with the data available to the authors and should be presented. However, given the methodological problems with the study, it may still be impossible to evaluate the authors' conclusions.

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BENJAMIN LIPTZIN, M.D.
DANIEL FRIEDENSON, M.D.
Springfield, Mass.

Dr. Strain and Colleagues Reply

SIR: We appreciate the comments of Dr. Morris and Drs. Liptzin and Friedenson. Dr. Morris has invited our attention to the issue of study design. First, the design was different at

the two study sites: Mount Sinai had a baseline nonintervention year compared to the intervention cohort (only one orthopedic unit), whereas Northwestern Memorial Hospital had a contemporaneous control (three orthopedic units) (table 2 in our article). Control and experimental observations were occurring during the same time period. Therefore, Dr. Morris's concern about nonspecific factors has been mitigated at the Northwestern site. Second, the demographic variables: age, sex, marital status, and seriousness of medical illness (Horn Severity of Disease Rating) were not significantly different between the baseline control and intervention years. Data analyses underway will answer Dr. Morris' third question as to whether or not the patients with treated psychiatric morbidity had a shorter length of stay in the experimental year. However, the nature of the liaison intervention could have impacted upon patients without frank psychiatric morbidity as well; e.g., problems of coping, disturbances of mood, families reluctant to take home an impaired elderly patient, changing long-acting hypnotics to short-acting forms, which permitted patients to attend morning physical therapy that may have otherwise been missed. Therefore, it would not have been expected that only patients with psychiatric and medical comorbidity would have shortened length of stay secondary to the liaison intervention.

Space limitations restrict addressing all the issues raised by Drs. Liptzin and Friedenson. Admission and discharge clinical assessments, i.e., clinician-evaluated *DSM-III-R* diagnoses and rating scales, were employed. The majority of the organic mental disorders were delirium (75%), and few were referred for psychiatric consultation. In contrast to the baseline year when psychiatric consultation was requested and provided to only 10% and 2% of the elderly hip fracture patients at Mount Sinai and Northwestern Memorial Hospital, respectively, the liaison screen during the intervention year resulted in psychiatric evaluation and treatment (if necessary) of 79% and 61% of the patients, respectively. Patient visits (average=2.4) in no way reflect the total system intervention of liaison psychiatry, which addressed the *denominator* (all the patients) rather than the *numerator* (only those referred). A *contemporaneous* control cohort at Northwestern was observed simultaneously with the intervention group that stayed 2 days less in two disparate hospitals.

Those outliers who were in excess of two standard deviations because of medical complications and/or new illnesses (e.g., myocardial infarctions, cerebral vascular accidents), were appropriately omitted from the sample.

All patients had Medicare or third-party insurance. The hospital was losing money on every patient who exceeded the diagnosis-related group (DRG) reimbursement of \$7,500, and costs and charges were two and three times this reimbursed rate. If the patient could be discharged sooner, the costs would more closely approximate the DRG reimbursement rate. Since orthopedic beds were at a premium at the two hospitals studied, decreased length of stay would permit more admissions and result in a decrease in the losses these patients were incurring for the hospital. The hospital does not need to reduce its variable costs by reducing staff, but rather by admitting more patients for a shorter length of stay. Psychiatrist-ordered tests were a rare event and had a negligible effect on the \$14,000 cost per patient.

The amount of psychiatric time for the study was 15–20 hours per week per hospital, funded by an NIMH grant. This could be covered by a fellow or junior attending psychiatrist employed half time at a cost of approximately \$25,000.

It is routine to report group means, which represent average change, to compare control and experimental results on stand-

ard measures of psychiatric status. The two groups were significantly different in the amount of time that passed between initial and discharge assessment. This difference required us to adjust the comparison between liaison and control conditions to compare the relative clinical efficiency. This adjustment cannot be accomplished on individual change scores due to the variation in length of stay within each group. Analysis of covariance, for instance, would be completely inappropriate in this case, due to the correlation between the length of stay and the independent variable (liaison versus control).

The department of orthopedics at the Mount Sinai Hospital is supporting the psychiatric screening of all elderly patients with traumatic injury on their service.

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Competency to Make a Will

SIR: I would like to present two thoughts that might be helpful to psychiatrists who are asked to perform a forensic consultation to assess competency to make a will (1):

1. It has been my experience that, according to the American Association of Psychiatry and Law, Ethical Guidelines, "A treating psychiatrist should generally avoid agreeing to be an expert witness or to perform an evaluation of his patient for legal purposes" (2). The role ambiguity and conflict, as well as the loss of both the confidentiality essential to a therapeutic alliance and the objectivity essential for a forensic consultation, can be best avoided by splitting such dual roles with the individual patient between two clinicians: the treating psychiatrist and the forensic psychiatrist (3).

2. Even with the organically impaired patient, psychodynamically driven affective factors such as pathological grief can be major influences on competency. When the forensic psychiatrist encounters such a case, referral for appropriate treatment and a subsequent reevaluation of competency is warranted (4).

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HAROLD J. BURSZTAJN, M.D.
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Dr. Spar and Dr. Garb Reply

SIR: We are grateful to Dr. Bursztajn for his valuable postscript to our article, in which space limitations precluded our addressing the relationship between the roles of consulting expert and

treating physician. Because of the likely breach of confidentiality entailed by expert testimony, as well as the need for expert objectivity, the treating physician is, as Dr. Bursztajn points out, generally a poor choice for this role. There are three exceptions: 1) if the expert contribution is limited to providing advice and consultation rather than testimony; 2) if the doctor-patient relationship has ended and the patient agrees to waive confidentiality; and 3) if litigation arises (as is frequently the case) after the patient's death. Although the question of objectivity remains in each of these cases, the greater weight afforded the opinions of an expert who has gained familiarity with the patient through a therapeutic relationship will frequently outweigh these concerns.

We also agree with Dr. Bursztajn that the expert may, at the discretion of the parties requesting the consultation, recommend various interventions, including psychiatric or general medical treatment. An interesting potential ethical dilemma for the expert is posed if the testator lacks testamentary capacity due to a treatable condition but the requesting parties are satisfied with the status quo and either do not ask for or reject recommendations for treatment!

J. EDWARD SPAR, M.D.
ANDREW S. GARB, J.D.
Los Angeles, Calif.

Suicide Among Homosexual Youth

SIR: The otherwise excellent review on suicide by Herbert Hendin, M.D. (1), fails to address the increased vulnerability of homosexual youth for suicide.

Several recent reports show this problem to be serious. Remafedi and Farrow (2) reported 41 suicide attempts among a sample of 137 gay and bisexual youth. Rotheram-Borus (unpublished report) studied three groups of minority youth and found that 28% of all subjects, but 41% of gay and bisexual subjects had attempted suicide. The United States Department of Health and Human Services (3) has stated that gay and lesbian youth are two to three times more likely to attempt suicide than other youth.

The formation of sexual identity is always characterized by sexual and emotional changes, but homosexual youth must also contend with widespread negative social attitudes. As a result, family and peer condemnation rather than support is often evident. Hetrick and Martin (4) reported that one-third of 329 gay adolescents had been subjected to violence because of their sexual orientation; 49% of this violence was at the hands of family members. Twenty percent of their subjects had either attempted suicide or had prominent suicidal ideation. In addition, many gay youths experience anxiety about the risk of HIV infection.

Homosexual youths are often unable to find someone knowledgeable with whom they can comfortably discuss these problems, including individuals who have successfully integrated a gay or lesbian identity. This may lead to overwhelming isolation and depression.

Youth suicide is now an epidemic and the object of national concern. Suicidal behavior among gay and lesbian youth is an epidemic within an epidemic that remains largely unknown. It is hoped that future contributions to the psychiatric literature on suicide will recognize and address this problem.

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STEVEN PRENZLAUER, M.D.
JACK DRESCHER, M.D.
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Dr. Hendin Replies

SIR: I agree with Dr. Prenzlauer and his colleagues in believing that the subject of suicide and attempted suicide among homosexuals requires special attention.

In my own studies of college students who made serious suicide attempts, I found, as did the authors cited by Dr. Prenzlauer and associates, a disproportionate number of male and female homosexuals among the suicide attempters. Their suicide attempts were usually precipitated by an overt rejection or abandonment by someone with whom they were currently involved. In every case there was a history of early maternal abandonment which was not present among homosexual students seen in our control group who were not suicidal (1, 2). Guilt or shame over being homosexual was not a significant factor in their suicidal behavior.

There is, however, some evidence based on questionnaire responses from individuals in homosexual college organizations and "rap" groups that suicidal ideation and past suicide attempts were influenced by social rejection for being homosexual in young men conflicted about their homosexuality (3). Evidence based on controlled studies that included homosexuals seen immediately after a suicide attempt is needed before any linkage between such experiences and suicidal behavior could be established. Although all homosexual young people have to contend with the negative social attitudes that Dr. Prenzlauer and colleagues describe, there is so far no evidence that suicidal homosexuals who have killed themselves have suffered more from these attitudes than nonsuicidal homosexuals or that such attitudes are a major factor affecting the suicide rate of homosexuals (4).

Studies of actual suicide have, so far, not confirmed that there is a greater incidence of homosexuality than to be expected among the suicides. The comprehensive Robins study based on data gathered originally in the late 1950s found no homosexuals among the 134 subjects of whom 103 were male (4). Accepting a male homosexual rate of 5% in the population (most estimates are greater), the finding is statistically so improbable ($p=0.005$) as to suggest that the greater concealment of homosexuality in that time period influenced the result.

The more recent comprehensive study by Rich et al. (5) concluded that the rate of suicide among homosexuals is not greater than that for heterosexuals. Significantly, all of the homosexuals in the Rich sample, were males in the age range between 21 and 42 years. That no homosexuals were present among the 83 men older than 42 years among the sample who killed themselves is also so improbable as to suggest that concealment may still be a factor affecting the figures in the older group. The need for concealment is of course a reflection of

the negative social attitudes that Dr. Prenzlauer and colleagues address.

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ADITYANJEE, M.D.
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HERBERT HENDIN, M.D.
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Multiple Personality Disorder: A Factual Error

SIR: J. Modestin, M.D. (1), quoted our work on multiple personality disorder in India (2) and attributed to us the hypothesis that the patients with the same "basic fault" in India are more prone to develop *hysterical psychosis* in comparison to multiple personality disorder in the United States.

We did speculate whether "possession syndrome" and multiple personality disorder represent the cross-cultural variants of the same dissociative disorder in India and the United States respectively, but we did not suggest the same about hysterical psychosis. Dr. Modestin seems to be unaware of the literature emanating from India on face and descriptive validity of possession syndrome (2-5) and naively substitutes it with "hysterical psychosis."

An informed awareness of the literature on both these entities would suggest that they are not the same. Possession syndrome certainly is a dissociative disorder seen in South Asia, but it is not a psychotic illness. We still reiterate our original hypothesis that the unavailability of the diagnostic category of "possession syndrome" and similar dissociative disorders in the current U.S. diagnostic system may be one of the reasons for overdiagnosis of multiple personality disorder in this country.

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Dr. Modestin Replies

SIR: The possession syndrome is known in many cultures (1). Even though it may take on special transcultural forms (2) and in that case, perhaps, represent a special culture-bound entity, it has always been considered an expression of hysteria or schizophrenia in most cases by Western psychiatrists (1, 3, 4). The immediate basis of my "naive substitution" of possession syndrome with hysterical psychosis is, however, the paper by Adityanjee et al. In that paper they themselves talk about "spirit possession—perhaps a form of *hysterical dissociation state*" and about "the documented high prevalence of *hysterical possession* in India [emphasis added]." So if they consider the possession syndrome to be different from hysteria, which, incidentally, has by no means been generally proven, they should be more careful in their own formulations. The descriptive criteria for a psychotic disorder, as defined, e.g., by Research Diagnostic Criteria (5), will most probably be met in the vast majority of "possessed" patients.

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Reprints of letters to the Editor are not available.

Annual Reports to the Membership

The following are edited versions of the annual reports by the APA Secretary, Treasurer, Medical Director, Speaker, and Speaker-Elect and the chairpersons of the APA Committee on Constitution and Bylaws, Committee on Membership, and Committee of Tellers. The reports were presented at the APA annual business meeting in Washington, D.C., on May 3, 1992.

Report of the Secretary: Summary of Actions of the Board of Trustees, May 1991–March 1992

Steven S. Sharfstein, M.D.

OVERVIEW

It is my personal and constitutional privilege as Secretary to report to the membership the actions taken by the Board of Trustees and some of the significant activities of the Association over the past year. A more specific summary of Board of Trustees actions follows this overview. Over the past year the Board addressed a variety of economic issues and concerns, including problems in managed care systems, rising health care costs, and governmental efforts (local, state, and national) to regulate or change health care systems.

Membership

Membership activity and fiscal policies. The total membership as of April 1, 1992, was 37,512, which is 1% higher than last year. While Members-in-Training continue to be the greatest source of General Members, the number of medical students entering psychiatry residencies has stabilized, and thus the overall increase in APA membership has flattened. The proportion of Members-in-Training within the APA membership increased from 6% in January 1980 to 15.8% in 1992. Residents are significantly involved in the activities and components of the Association, including having a voting and a nonvoting member on the Board of Trustees and a representative and deputy representative from each of the seven Area councils within the Assembly. In addition, the Committee of Residents and Fellows and the resident fellowship programs have representation on the Board. The Committee of Early Career Psychiatrists focuses on the needs and interests of psychiatrists who have just completed their residencies.

In 1990 an ad hoc committee on membership and fiscal policies predicted a slower rate of growth of income from member dues, attributing this decrease primarily to the rapid growth in the number of members who would become dues exempt. Under the "rule of 95" a member reaches Life status when the member's age and number of years of membership total 95. To date, reaching Life status has been equivalent to becoming dues exempt. This spring APA members approved an amendment on the 1992 ballot that modifies the dues-exempt status so that members who achieve Life status in 1993 and thereafter will be required to pay reduced dues for 10 additional years. Life Members/Fellows will be billed for two-thirds of the highest dues

rate for the first 5 years after they achieve Life status and one-third of the highest dues rate in the succeeding 5 years. Thereafter, Life Members/Fellows will be exempt from dues payments. In addition to recommending this modification in dues-exempt status, the ad hoc committee recommended that APA offer members the option of paying dues in a lump sum (i.e., paying the full amount of dues that they would have paid over the remaining years of their dues-paying status). After the Budget Committee and the Committee on Membership delineated fiscal and administrative details for enacting such a plan, the Board approved this recommendation.

Membership directory. In February 1992 a subcommittee of the Committee on Membership met to explore issues related to publishing a membership directory. The subcommittee explored various options for conducting a survey that would obtain the needed information. The subcommittee agreed that a new membership directory (not a biographical directory) was needed by no later than 1994. The Board approved producing the directory and authorized the Committee on Membership to develop a budget and seek outside funding for the project.

Member benefits. The APA Purchasing Group, Inc., continues to enhance its ability to monitor and control APA-sponsored insurance programs. Through careful management and innovation, it has been able to hold the line on malpractice premiums: the APA-sponsored professional liability insurance program announced lower premiums for many policyholders for the 1992–1993 policy year. The rates for program participants decreased about 2% on average. Important modifications were made to the experience rating program, introduced last year and designed to offset the effects of adverse selection (in which the members with the lowest risk abandon the program for less expensive, competing policies, leaving the APA-sponsored program with higher average losses and fewer insureds, who then must pay higher premiums). Responding to member concerns about the threshold for determining what is a significant claim, the APA Purchasing Group agreed that regional variability of suit cost is important and took action to replace the nationwide \$20,000 threshold for defining significance. The thresholds for the 1992–1993 year are tied to premium level, which varies from \$20,000 to \$50,000, depending on location. The APA Purchasing Group will continue to study the effect of previous claims on future losses to evaluate the impact of the experience rating system on the program in the long term.

In recognition of the loss experience of the past 5 years and changes in program enrollment, rates were reduced in a number of states. Premiums remained at 1991-1992 levels in 28 states and fell in 20 states and the District of Columbia. California members' premiums are based on a new regional rating system; some California members' premiums have remained at the 1991-1992 level, while others have decreased from 14% to 48%, depending on rating district. Only one state, Texas, has seen higher rates in the 1992-1993 policy year, increasing either 5% or 15%, depending on locale.

Participation in APA's catastrophic health insurance program continues to fall. The basic premium was increased by 30% for the 1992-1993 policy year, mirroring the experience of most commercial health insurance programs. The Committee on Member Life, Accident, and Health Insurance continues its careful review of the performance of the catastrophic health insurance program to determine what changes may be warranted. In November 1991 many participants in the APA-sponsored disability and life insurance program received premium refunds. The refunds, based on effective date of coverage and amount of insurance, were due to the favorable loss experience of the disability and life insurance program.

APA/district branch activity. Traditionally, APA components and staff interact with the district branches, supporting their membership and governance efforts and working through the public affairs and legislative networks. This past year the Board gave considerable attention to the potential district branch expenses of covering the deductible of the directors and officers insurance. APA carries directors and officers insurance for the national society and for the district branches and state societies and assumes the deductible (\$200,000) for all ethics activities. The Board extended its assumption of the deductible in claims against its district branches and state societies arising out of actions affecting membership status or other activities undertaken at the written request or direction of APA. In addition, the Board approved an APA/district branch cost-sharing plan for paying additional portions of the deductible in cases that are not covered by any other arrangements; the cost-sharing plan incorporates a flat fee plus a differential based on the size of the district branch.

Ethics

The Ethics Committee continues to provide educational programs to assist district branches with the new procedures for handling complaints of unethical conduct that were implemented in October 1989. In 1990-1991 an ad hoc committee reviewed the composition and procedures of the Ethics Appeal Board, reporting to the Assembly in May 1991 and to the Board in September 1991. The Board approved a change in the composition and tenure of the Ethics Appeal Board, which will provide greater interaction among district branches and the appeals process, as well as greater flexibility for the President in making appointments to the Ethics Appeal Board.

In March 1992 the Board recommended development of an amendment to the APA Constitution and Bylaws regarding members who resign during ethics complaints, and it asked the Committee on Constitution and Bylaws to prepare wording for the amendment. An amendment to the Bylaws will be read to the membership at this annual business meeting for placement on the 1993 ballot. The amendment will permit APA to report to the membership and the National Practitioner Data Bank the name of a member against whom an ethics complaint is filed within 90 days of his or her resignation.

Public Affairs

APA's "Let's Talk About Mental Illnesses" campaign moved into its 5th year, continuing to reach millions of Americans with positive messages about mental illnesses and the effectiveness of psychiatric diagnosis and treatment. The film, workshop, and exhibit components of the campaign were supported by an unrestricted educational grant from the Upjohn Company. The three films (on panic disorder, anxiety disorder, and depression) have been seen 98.5 million times through direct APA distribution, distribution by Modern Talking Pictures, and through local and national television broadcast. The third film, "Depression: The Storm Within," won a CINE Golden Eagle Award, the most prestigious award for a documentary next to an Oscar, from the Council on International Nontheatrical Events. The

film is now eligible for entry in international film festivals and in the Academy Awards. The campaign's prize-winning workshop "Panic Disorder: Diagnosis, Treatment, and Management" has benefited 21,210 physicians and other health professionals, and the Division of Public Affairs' exhibits have been seen by 234,000 health professionals at 57 national meetings. During the year the Division of Public Affairs published new mental illness awareness guides for the media and health professionals (similar to earlier guides for clergy and educators). Wide distribution of the media guide was made possible through a much-appreciated grant from the American Psychiatric Foundation.

Joint Public Affairs and Government Relations Activities

Mental Illness Awareness Week. Each year the APA Division of Government Relations, with the help of the membership, contacts members of Congress to press for legislation in recognition of Mental Illness Awareness Week. In 1991 APA initiated the week (October 6-12) by hosting a breakfast on Capitol Hill, jointly convened with the newly formed Congressional Task Force on Mental Illness. The featured speakers included former Houston Oilers and National Football League Hall of Fame running back, Earl Campbell, who spoke of his personal experiences with panic disorder, and Dr. Freda Lewis-Hall, who spoke on psychiatric treatment of panic disorder. Almost all of district branches sponsored activities commemorating Mental Illness Awareness Week, during which APA sponsored a successful National Depression Screening Day, organized by Dr. Douglas Jacobs of Harvard University. Screening days were held at more than 100 sites in all 50 states, attracting over 5,000 participants (50% of whom were recommended for follow-up). Currently APA is working with Senator Paul Simon and Representative Ron Wyden to obtain introduction of the 1992 Mental Illness Awareness Week resolution in the Senate and House of Representatives.

Joint State Legislative and Public Affairs Institute. APA produced the first Joint State Legislative and Public Affairs Institute, held in Bal Harbour, Fla., Feb. 27 to March 1. The 4-day program attracted over 400 APA members, APA Auxiliary members, district branch executives, lobbyists, public affairs consultants, guests, and spouses. Participants represented 69 of the 76 district branches. The topics covered during the institute included managed care, access to care, nonphysician prescribing, media relations, and *Physicians' Current Procedural Terminology* (CPT) codes. In addition to learning of innovative developments around the country, the participants were instructed on lobbying strategy and media skills for more effective advocacy. The participants overwhelmingly urged continuation of the joint institute.

Government Relations

Many key issues for psychiatrists and patients were addressed throughout the past year. Highlights of some of the issues follow.

Access to health care. The Board of Trustees gave considerable attention to access issues. The prospects for health care reform are more confused and perhaps more remote in the short term than ever. President Bush joined the debate on health care reform by unveiling his own set of proposals, focusing chiefly on reform of the health insurance market. The Senate approved similar reforms as part of a larger tax and economic recovery bill; those health care reform provisions were, however, stripped from the tax bill in conference with the House of Representatives and deferred for possible consideration later as separate legislation. APA continues efforts to work with Congressional committees to improve coverage of treatment for mental disorders in all health care reform legislation. APA has managed to ensure that most of the key proposals for health care reform include at least some coverage of psychiatric services, although typically limited in scope and duration (primarily because of perceptions that coverage of psychotherapy and counseling is not a basic necessity or a medically necessary service). Comprehensive health care reforms may still be several years away.

Reorganization of and appropriations for the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA). The Board discussed Senate-approved legislation to reorganize ADAMHA, shifting the three institutes' research activities to the National Institutes of

Health while maintaining a separate services agency (Alcohol, Drug Abuse, and Mental Health Services Administration). In June 1991 the Board agreed to not support the reorganization of ADAMHA until it had consulted with other constituency groups. In December the Board continued to have serious reservations about the proposed reorganization, pledging to work to ensure that any outcome would be in the best interests of the mentally ill.

International medical graduates (IMGs). APA worked with the American Medical Association (AMA) in persuading both houses of Congress to pass legislation that, when implemented, will establish the AMA National Credentialing Verification Service as a repository for medical education and residency records. The legislation provides long-sought protection against discrimination against IMGs, as well as the assurance that patients will receive medical treatment from qualified and licensed physicians. The bills are fairly similar: they call for a federal study to determine whether IMGs experience higher rejection rates and longer waits for medical licensure. Both bills would provisionally recognize the AMA's new National Credentialing Verification Service as a way for IMGs to reduce the extra paperwork for licensure and hospital privileges. Although legislation has passed both the House and Senate, the date of the conference has not yet been set.

"Medigap" insurance regulations. APA efforts produced a major victory by ensuring that Medicare supplemental ("Medigap") insurance plans cover the current 50% beneficiary copayment for Medicare outpatient mental health treatment. The Omnibus Budget Reconciliation Act 1990 budget bill required the National Association of Insurance Commissioners to substantially revise its model regulation for Medigap insurance. APA has been pressing the Congress since August 1990, and the National Association of Insurance Commissioners since the spring of 1991, to make certain that the revisions explicitly require all Medigap policies to cover the full amount of the 50% beneficiary copayment for outpatient mental health care under Medicare. The National Association of Insurance Commissioners recently confirmed to APA that its revised model regulation does include such a coverage requirement.

Medicare fee schedule. In June 1991 APA was shocked and disappointed when the Health Care Financing Administration (HCFA) released its long-awaited proposal for a resource-based relative value scale (RBRVS); the drastic cuts were in stark contrast to what had been forecasted by the Hsiao team at Harvard University. While the cuts were of concern to all of medicine, they had a particular impact on psychiatry. APA responded to specific problems in the HCFA's initial proposal for the Medicare fee schedule. Before releasing the RBRVS Medicare fee schedule in late November, the HCFA increased the work relative value units for psychiatric services. While this change substantially improved the fees for psychiatric services over those originally proposed in June, the Board recognized that the overall impact on psychiatrists' fees, particularly for those practicing in high-cost urban areas, would be negative. APA is continuing to respond to the outpouring of concern from psychiatrists.

Psychologist hospital and prescribing privileges. The first group of clinical psychologists will soon enter their second year of training under the U.S. Department of Defense demonstration program for psychologist prescribing privileges training. They will not be permitted to prescribe independently. APA learned that some of the psychologists in the program were faring so poorly on the examinations for their courses that they asked to be permitted to audit the courses rather than receive specific grades. APA is now working with concerned members of Congress to call attention to this development and to press Department of Defense officials for a full explanation. With the vigorous support of the California and Texas district branches, APA helped persuade the Senate not to approve a bill that would have amended the Medicare part A conditions of hospital participation to permit clinical psychologists to care for inpatients receiving qualified psychologist services. At the state level, legislation on psychologist hospital privileges has been under consideration in 10 states. In 1991 Ohio enacted legislation that permits psychologists to be on hospital staffs but prohibits their having admitting privileges.

Student indebtedness. Although no final action was taken in 1991, the House Education and Labor Committee and the Senate Labor and Human Resources Committee each approved legislation that included provisions to end the current 2-year deferment of repayment of stu-

dent loans by medical residents. Both bills would provide residents with forbearance on their loans, but such loans would continue to accrue additional interest during the forbearance period. It is not possible to predict what the final conference product will be, and informed sources say that the bill may be almost entirely rewritten in conference. APA, with strong support from its Members-in-Training, continues an aggressive lobbying effort to restore the deferment.

Economic Affairs and Practice Activities

Managed care. Issues related to managed care have been discussed widely throughout APA over the past year. Members used the toll-free "hot line" to help identify egregious practices. Well-documented cases, as well as generic issues, were and are being discussed with the leaders of a number of utilization management companies. These meetings are convened under the auspices of the Committee on Managed Care within the Council on Economic Affairs. This communication has included dialogue with a major employer, which has accepted most of APA's comments on broad guidelines for utilization review for its employees. As recommended by the Assembly, the Board also adopted guidelines to be used when APA reviews industry criteria for standards of care.

During 1991-1992 APA has developed a number of documents related to managed care. The Committee on Managed Care published *Utilization Management: A Handbook for Psychiatrists*, which is being distributed on request through the 76 district branches. APA also published a new *Manual for Psychiatric Quality Assurance*, which includes a historical overview of APA's efforts to ensure appropriate care for patients. The Conference on Ethics for Psychiatry in Managed Care, sponsored by the Ethics Committee and the Committee on Managed Care, was held in October 1991. The conference probed the ethical dilemmas psychiatrists face as health insurers intensify efforts to manage mental health care benefits. The conference proceedings are being edited for publication.

Broader ethical issues in the delivery of psychiatric services are being studied by the ethics, managed care, and other committees. The Board did not endorse guidelines developed by the National Association of Private Psychiatric Hospitals. The Board directed APA to develop its own criteria for psychiatrists working in both public and private organized systems of care and, in March 1992, approved hospital admission procedures for psychiatrists.

For more than a year an Assembly ad hoc task force on managed care gathered information about membership support around the country for a variety of strategies to cope with problems found in managed care systems. In addition to geographic representation, the task force included minority and younger members to ensure incorporating their views. A preliminary task force report, first discussed by district branches, was considered by the Assembly in November 1991. In December 1991 the Board adopted the four types of strategies identified by the task force and endorsed by the Assembly: 1) legislative/regulatory, 2) market force influence, 3) consultative, and 4) judicial. APA is currently involved in the first three strategies, and district branches are engaged in legislative and regulatory matters. The Board asked the Committee on Managed Care to study and make recommendations about the specific proposals in the Assembly task force report.

A managed care network, similar to the public affairs and legislative networks, is being developed and will meet during the 1992 annual meeting. Each district branch has been asked to inform the APA Office of Economic Affairs of its local contact for the network. The Connecticut Psychiatric Society had, through voluntary contributions, collected over \$25,500, which it donated to APA for a litigation effort. Since APA apparently would not be using these funds for this specific purpose in the near future, the Board voted to return the money with its deep appreciation. The Board also expressed its appreciation to the Assembly for its considerable efforts in determining membership opinion and for its excellent report on recommended APA strategies with respect to handling problems in the managed care arena.

CPT-4. The Work Group on Codes and Reimbursements and the Office of Economic Affairs have worked to educate the membership about the newly established evaluation and management codes published in CPT-4 and about other significant changes in Medicare re-

imbursement. Several workshops have been presented around the country by Drs. Chester Schmidt and Tracy Gordy. Additionally, a workshop and a course will be presented at the 1992 annual meeting. A letter was sent to the nation's major insurers explaining the new interactive psychiatric medical codes, with explanations and examples of their use. Sample psychiatric vignettes, representing the new codes for inpatient and outpatient visits, have been made available to members. The Work Group on Codes and Reimbursements and the Office of Economic Affairs have continued to monitor the difficulties and concerns of members in regard to the new codes, with special emphasis on reimbursement by Medicare.

Research

DSM-IV. Work on *DSM-IV* continued at a strong pace. Draft criteria for each proposed diagnostic category were developed and distributed widely for comment in *DSM-IV, Work in Progress: Options Book*. A series of columns on *DSM-IV* were published in the *Hospital and Community Psychiatry* journal. Numerous activities related to *DSM-IV* are planned for this annual meeting, and field trials are being completed to assess specific nosologic issues. The National Institute of Mental Health is sponsoring a major meeting on *DSM-IV* and *ICD-10* in July 1992.

During the November 1991 Assembly APA received notice of a petition asking APA to hold a referendum on adopting *ICD-10*, after its publication, as the official psychiatric classification system in the United States and delaying the publication of *DSM-IV* at least until 1997. The petition fell short of the requisite 500 signatures of voting members, but the petitioners may resubmit a petition for a referendum on this issue for the 1993 ballot. In March 1992 the Board of Trustees affirmed the policy that signatures on a petition are valid only for the year in which the petition is initially submitted, and the Board stated that the petitioners must resubmit a new petition with the requisite number of current signatures if they wish the referendum to be on the ballot in the 1993 election.

Practice guidelines. Under the aegis of the APA Steering Committee on Practice Guidelines, practice guidelines are being drafted by psychiatrists in active clinical practice and are circulated for comments before coming to the Assembly and Board for approval. Two practice guidelines (for eating disorders and major depression) are in the final stages of consideration, and six others are in earlier stages of development. As a member of the AMA/Specialty Society Practice Parameters Partnership, APA has participated in developing criteria for practice guidelines for all of medicine. APA has also participated in an Institute of Medicine field testing of a preliminary guideline instrument. In May and June 1992 the Assembly and the Board will be considering for approval the APA-developed practice guidelines for eating disorders. Members are encouraged to participate in the development of these guidelines.

American Psychiatric Foundation, Inc.

Since its incorporation in 1990, the American Psychiatric Foundation, Inc., has continued to enhance the fund-raising objectives of the Association. The members of the Foundation's interim Board of Directors are Drs. Elissa P. Benedek (President), Carolyn B. Robinowitz (Executive Vice President), Mary Jane England (Secretary/Treasurer), Robert S. Garber, Edward Hanin, Lawrence Hartmann, Clifford Parish, Jr., G. Thomas Pfafchler, Howard Wallach, and Melvin Sabshin (ex officio). The organizational steps that have been taken include finalizing the application for recognition as a tax-exempt organization, which outlines activities the foundation may pursue in public education, research, professional development, and special projects. In addition, a business plan detailing programs and funding for the foundation has also been prepared. Corporate constituents are being invited to participate in the new Corporate Advisory Council. To date, the foundation has made contributions to the National Museum of Health and Medicine (\$10,000), the APA Division of Public Affairs for Mental Illness Awareness Week (\$10,000), the APA Library for automation of the card catalogue (\$16,000) and for reference acquisitions (\$3,000), the Manhattan Homeless Project (\$5,000), and the APA Award for Research (\$2,500/year, as seed money, for 5 years). The APA Board of Trustees approved expanding membership solicitation activities from primarily APA Life Members and Life Fellows to all APA members.

Conclusion

Every member of APA is welcome to attend meetings of APA components (except meetings of the Ethics Committee and Ethics Appeals Board or when a component goes into executive session). Your strong support is deeply appreciated; your recommendations for consideration by the Board or other components are most welcome.

Thank you for the privilege and honor of serving as your Secretary for the past year. I look forward to working with you to meet the challenges we face and opportunities we have during the coming year.

SUMMARY OF ACTIONS

The actions of the Board of Trustees are grouped by topic, and the topics are arranged alphabetically. The date of each action is given in parentheses at the end of the action. Complete wording and discussion of actions can be found in the minutes of the Board of Trustees.

Addiction

1. Approved the "Position Statement on the Care of Pregnant and Newly Delivered Women Addicts" (1) (approved by the Assembly in November 1991) (June 1991).
2. Authorized the Council on Addiction Psychiatry to explore the possibility of APA participation in the National Training System's initiative for a continuing education training project for psychiatrists that would focus on prevention and early identification of alcohol and other drug abuse problems (June 1991).
3. Adopted an APA policy against tobacco use and in support of voluntary discontinuation (June 1991).

Aging

1. Approved the report of the Task Force on Ethnic Minority Elderly for publication as part of the APA task force report series, subsequently discharging the task force and establishing the five-member Committee on Ethnic Minority Elderly within the Council on Aging (June 1991).
2. Approved the "Position Statement on Medical Use of Psychotherapeutic Medications in the Nursing Home" (Dec. 1991).

AIDS

1. Voted to promote the policy that a history of substance abuse should not preclude adequate treatment of substantial physical pain in AIDS patients (Dec. 1991).
2. Approved, as an official APA policy, a statement on HIV infection and impairment of personal, social, or occupational functions (approved by the Assembly in November 1991) (June 1991).
3. Adopted as APA policy the revised "AIDS Policy: Guidelines for Inpatient Psychiatric Units" (2) (Dec. 1991).
4. Adopted as APA policy the revised "AIDS Policy: Guidelines for Outpatient Psychiatric Services" (3) (Dec. 1991).
5. Voted to adopt as APA policy, subject to approval by the Assembly, the revised "AIDS Policy: Position Statement on HIV Infection" (Dec. 1991).
6. Adopted as APA policy, subject to approval by the Assembly, the revised "AIDS Policy: Position Statement on HIV and Discrimination" (Dec. 1991).

American Board of Psychiatry and Neurology

1. Approved the nomination of Dr. Lenore Terr for a second 4-year term on the Board of Directors of the American Board of Psychiatry and Neurology (ABPN), beginning January 1992 (June 1991).
2. Voted to forward the names of Drs. Elizabeth Weller, John Kemph, and Barry Nurcombe to the ABPN as the APA nominees for members of the ABPN Committee on Child Psychiatry (Dec. 1991).

American Journal of Psychiatry

1. Extended the tenure of three Associate Editors whose terms were completed in May 1992 (two of whom were eligible for reappointment) to permit the new Editor of the *Journal* to recommend (re)appointments (March 1992).

American Medical Association

1. Authorized APA's participation in the AMA Specialty Society Process to Develop Relative Values for New or Revised CPT Codes (May 1991).

2. Endorsed the AMA Coalition of Physicians Against Family Violence, authorizing the President to appoint APA representatives to the coalition, as requested, and agreeing to support the costs of sending these representatives to the meetings (March 1992).

3. Endorsed the AMA position on managed care (Dec. 1991).

4. Approved an APA resolution asking that the AMA Young Physicians Section consider a change in the current bylaws that would replace the term "young physicians" with "physicians recently completing residency or fellowship training" (Dec. 1991).

American Psychiatric Foundation

1. Ratified the Executive Action taken by the President, Speaker, and Dr. Carolyn Robinowitz, Acting Medical Director, to appoint Mr. Clifford Parrish, Jr., to serve on the Board of Directors of the American Psychiatric Foundation, Inc. (Dec. 1991).

2. Voted to allocate the following monies from contributions to the American Psychiatric Foundation: a) up to \$16,000 to the APA Library for the automation of reference sources and development of an on-line card catalogue system (from the Fund for the Future), b) \$10,000 to fund the production and distribution of the Mental Illness Awareness Week literature (from the Fund for the Future), and c) \$3,000 for APA Library reference acquisitions (from the APA Tribute Fund) (Sept. 1991).

3. Endorsed the following allocations by the American Psychiatric Foundation: a) \$5,000 to assist with program costs of the Manhattan Homeless Project and b) \$500/year for 5 years to the APA Award for Research in Psychiatry to serve as a monetary expression of support (March 1992).

4. Voted in principle that past and future contributions to the APA Pooled Income Fund should be designated for the sole benefit of the American Psychiatric Foundation (March 1992).

5. Authorized the American Psychiatric Foundation to accept \$25,000 from the Sarnat family to support the 1992 Rhoda and Bernard Sarnat Mental Health Award, to be given in recognition of significant and far-reaching contributions to the advancement of mental health by an individual, group, or organization, without regard for professional discipline or nationality (June 1991).

6. Voted to release to the American Psychiatric Foundation the list of current annual meeting exhibitors to permit solicitation of them into the Corporate Partners program (Sept. 1991).

7. Approved a solicitation of APA members by including a check-off box for voluntary contributions on all member dues statements, with the understanding that this mechanism would be reviewed within a year of implementation to determine its impact (March 1992).

American Psychiatric Press

1. Approved the reappointment of Dr. Doyle Carson and the appointment of Dr. Lawrence Hartmann to 4-year terms on the Board of Directors of the American Psychiatric Press, Inc. (APPI) (May 1991).

2. Authorized the Medical Director to terminate APA's contract with Martin Publishing, which produces "Dialogue," if and when it seems appropriate, in view of APPI's negotiations to produce and market a newsletter for laypersons (March 1992).

Annual Meeting

1. Approved accepting outside support from a pharmaceutical company to provide box lunches for participants in a course on com-

munity resources for the homeless scheduled for the 1992 annual meeting (March 1992).

2. Increased the fee for industry-sponsored symposia at annual meetings from \$25,000 to \$30,000, beginning with the 1993 annual meeting (Dec. 1991).

3. Extended the application of the revised guidelines for pharmaceutical or other industry-sponsored symposia to the Institute on Hospital and Community Psychiatry, beginning with the 1992 institute; further, voted that all requests for revisions to the guidelines must be referred to the Committee on Advertisers and Exhibitors and be made in conjunction with the program committees for both the annual meeting and the H&CP institute (Sept. 1991).

4. Authorized the Committee on Psychological Aspects of Nuclear Issues to seek outside funds, following established procedures and working in conjunction with the Medical Director's office, to cover travel expenses for five guest speakers for a symposium at the 1993 annual meeting (Dec. 1991).

5. Authorized Dr. Herbert Sacks to seek outside funding, following established procedures and working in conjunction with the Medical Director's office, to support travel expenses of speakers and an honorarium for one speaker who will participate in the symposium "Anne Sexton, Poet and Patient" at the 1992 annual meeting (March 1992).

6. Authorized the Consortium on Public Psychiatry to seek outside funding, following established procedures and working in conjunction with the Medical Director's office, from the National Institute of Mental Health (NIMH) to sponsor a workshop at the 1992 annual meeting, jointly planned by the consortium, NIMH, and the National Alliance for the Mentally Ill, that would focus on improving psychiatric services in public programs (Sept. 1991).

7. Authorized APA to receive funding from NIMH (approximately \$3,000) to cover the costs of setting up a meeting of mental health services researchers to be held during the 1992 annual meeting (Sept. 1991).

8. Voted to suspend (commencing with the 1992 annual meeting) the solicitation and display of scientific exhibits at annual meetings and H&CP institutes (Sept. 1991).

9. Approved the following policy for selection of APA meeting sites: APA will consider any significant conflict between a state's laws or policies and corresponding policies/positions of APA, and APA's policy positions will be weighed in making these decisions; further, agreed that if APA decides to meet in a restrictive state (e.g., anti-choice), APA will consider constructive ways to educate the public and to advocate for APA's position during the meeting (June 1991).

10. Approved holding APA annual meetings at the following sites: Miami in 1995, New York City in 1996, San Diego in 1997, and Toronto in 1998; further, voted to encourage Mr. George Campbell, Director of the Office of Meetings Management, to report to the Board in December 1991 or March 1992 additional suggested sites for future annual meetings (Sept. 1991).

11. Authorized the Committee on Women, following established procedures and working in conjunction with the Medical Director's office, to seek outside funding of approximately \$10,000 to support a women's activity center at the 1992 annual meeting (June 1991).

12. Authorized the Committee on International Medical Graduates to seek approximately \$5,000 in outside funding, following established procedures and working in conjunction with the Medical Director's office, to support a reception for young international medical graduates and leaders of various ethnic groups at the 1992 annual meeting (Dec. 1991).

13. Authorized the Committee of Young Psychiatrists to seek outside funding (approximately \$12,000), following established procedures and working in conjunction with the Medical Director's office, to support a roundtable session for young psychiatrists at the 1992 annual meeting (Dec. 1991).

Awards

1. Authorized the Committee of Asian-American Psychiatrists, following established procedures and working in conjunction with the Medical Director's office, to seek outside funding of \$7,500 to sponsor a reception in honor of Dr. Kun-Po Soo at the 1992 annual meeting, with the understanding that the conditions for receipt of the funding must be consistent with APA policy (June 1991).

2. Authorized publication of a brochure publicizing the Asian/Asian-American Award (Dec. 1991).
3. Authorized the Committee on History and Library, following established procedures and working in conjunction with the Medical Director's office, to seek approximately \$7,000 in outside funding to support the Benjamin Rush Lectureship (June 1991).
4. Approved the following recipients of the APA Distinguished Service Awards to be presented at the 1992 annual meeting: Drs. Eli Robins and Albert J. Solnit for the individual awards and the Carters' Habitat for Living for the institutional award (providing that either or both of Jimmy and Rosalyn Carter could attend the annual meeting to receive the award) (Dec. 1991).
5. Ratified an Executive Action taken by the President, Speaker, and Medical Director to approve the American College of Neuropsychopharmacology as a recipient of the 1992 APA institutional Distinguished Service Award (March 1992).
6. Approved changing the description of the Human Rights Award to include "from any country" after the words "predominantly humanitarian or professional ones" and to authorize presentation of the award in 1992 (June 1991).
7. Approved the establishment of the William Sorum Award (June 1991).

Components—Discharged

1. *Board of Trustees components*: Ad Hoc Committee on the Annual Business Meeting and Forum (June 1991); Ad Hoc Task Force on Conflicts of Interest (March 1992); Ad Hoc Committee to Develop a Slate of Candidates for Election to the ABPN (June 1991); Ad Hoc Committee on Managed Care Issues (June 1991); Ad Hoc Committee to Revise Procedures for Nominating the MITTE (June 1991).
2. *Council on Aging*: Task Force on Ethnic Minority Elderly (June 1991).
3. *Council on International Affairs*: Task Force on APA Liaison With the World Psychiatric Association (Dec. 1991).
4. *Council on Medical Education and Career Development*: Task Force on Post-Residency Fellowship Training Programs (June 1991).
5. *Council on Psychiatry and Law*: Task Force on Disclosure of Psychiatric Treatment Records in Child Custody Disputes (Dec. 1991).
6. *Council on Research*: Task Force on Tardive Dyskinesia (Dec. 1991); Task Force on Quantitative Electrophysiological Assessment (Dec. 1991).

Components—Established

1. *Board of Trustees components*: Ad Hoc Committee on APA Legal Representation (June 1991); Ad Hoc Committee to Develop a Slate of Candidates for Election to the ABPN (Dec. 1991); Ad Hoc Committee on Membership Losses (June 1991); Ad Hoc Committee to Review the Ethics Appeals Board (this is a joint Board of Trustees and Assembly component to review the Ethics Appeals Board every 4 years, i.e., the first ad hoc committee would be appointed in 1994 for the 1995–1996 cycle) (Sept. 1991); Task Force to Review Medical Necessity and Reimbursement Criteria for Use by Managed Care Organizations and Payers of Psychiatric Care (joint Board of Trustees and Assembly component) (June 1991).
2. *Council on Addiction Psychiatry*: Task Force on Nicotine Dependence (Dec. 1991).
3. *Council on Aging*: Committee on Ethnic Minority Elderly (June 1991); Work Group on Model Standards for Long Term Care Insurance (established June 1991, funded Dec. 1991).
4. *Council on Medical Education and Career Development*: Work Group on Accreditation and Certification (Dec. 1991).
5. *Council on Psychiatry and Law*: Task Force on Peer Review of Psychiatric Testimony (Dec. 1991).

Components—Modified

1. *Constitutional components*: Established a subcomponent of the Committee on Membership to study the feasibility of producing a directory of members (Dec. 1991) and then authorized the subcomponent to produce a membership directory (March 1992).
2. *Special boards and commissions*: a) Approved 3-year staggered

tenures for members of the Commission on AIDS, with the understanding that each member could be reappointed once, and authorized annual appointment of the chairperson of the commission (June 1991); b) expanded the charge and membership of the Commission on Subspecialization to include liaison with the Committee on Graduate Education (within the Council on Medical Education and Career Development) and with the Residency Review Committee for Psychiatry of the Accreditation Council for Graduate Medical Education (June 1991 and Dec. 1991); c) changed the membership of the Ethics Appeals Board to include two past Presidents, a past Speaker of the Assembly, the chairperson of the Ethics Committee, and a chairperson of a district branch ethics committee, with the Secretary continuing as chairperson; tenure for members was set at 3 years, and it was requested that members selected to serve on the Ethics Appeals Board have had ethics committee experience (at either the local or national level) and be strongly committed to the ethics process (Sept. 1991).

3. *Council on Children, Adolescents, and Their Families*: Extended the tenure of the Task Force on Day Care for Preschool Children to December 1993 to permit the task force to monitor proposed day care legislation (Dec. 1991); transferred the Blanche F. Ittleson Award Board from the Council on Internal Organization to the Council on Children, Adolescents, and Their Families (Dec. 1991).

4. *Council on Economic Affairs*: Authorized the transfer of the Committee on Private Practice from the Council on Psychiatric Services to the Council on Economic Affairs, with the understanding that there would be liaison with the Council on Psychiatric Services (no change in the committee's charge) (March 1992).

5. *Council on Internal Organization*: Changed the name of the Foundations' Fund Prize to the APA Research Award (Dec. 1991); transferred the Blanche F. Ittleson Award Board to the Council on Children, Adolescents, and Their Families (Dec. 1991); transferred the Marie H. Eldredge Award Board to the Council on Psychiatric Services (Dec. 1991); changed the name of the Personnel Committee to the Committee on Human Resources (June 1991).

6. *Council on Medical Education and Career Development*: Expanded the charge of the Committee on Graduate Education to include responsibility for all future activities related to subspecialty fellowship training, in collaboration with the Commission on Subspecialization, and, further, to include liaison with the Commission on Subspecialization and conveyance of information regarding all applications for certification of added qualifications (June 1991 and Dec. 1991); changed the name of the Task Force on Educational Activities for Diagnostic Systems to the Task Force on Diagnostic Education (no change in the charge) (Dec. 1991); changed the name of the Committee of Young Psychiatrists to the Committee of Early Career Psychiatrists (no change in the charge) (Dec. 1991).

7. *Council on National Affairs*: Revised the charge to the Committee of Black Psychiatrists (Dec. 1991); changed the name of the Committee of American Indian and Alaskan Native Psychiatrists to the Committee of American Indian, Alaska Native, and Native Hawaiian Psychiatrists and authorized an addition to the membership of the committee to include a representative of Native Hawaiian psychiatrists (Dec. 1991).

8. *Council on Psychiatric Services*: a) Authorized the Council on Psychiatric Services in December 1990, by Board approval of an action paper from the Assembly, to establish a consortium on public psychiatry; by June 1991 the consortium included representatives from the Committee on Disability and Rehabilitation, the Committee of State and Community Psychiatry Systems, the Committee on Chronically Ill and Emotionally Handicapped Children, the Task Force on Geriatric Psychiatry in the Public Mental Health Sector, the Task Force on the Homeless Mentally Ill, the Assembly Committees on Public Psychiatry and on Community Psychiatry and the State/University Collaboration Project; in December 1991 the Board authorized inviting representatives from the following additional components to join the consortium on public psychiatry: the Committee on Veterans' Affairs, the Committee on Psychiatric Services in Jails and Prisons, the Committee on Psychiatric Services in the Military, the Committee on Psychiatric Services to the Mentally Retarded/Developmentally Disabled Persons, and the Assembly Committee of Representatives of Minority/Underrepresented Groups; b) expanded the charge of the Council on Psychiatric Services to permit it to directly

invite groups to join the consortium on public psychiatry as the council sees appropriate (Dec. 1991); transferred the Marie H. Eldredge Award Board from the Council on Internal Organization to the Council on Psychiatric Services (Dec. 1991); transferred the Committee on Private Practice from the Council on Psychiatric Services to the Council on Economic Affairs, with the understanding that there would be liaison with the Council on Psychiatric Services (no change in the charge) (March 1992).

Components—Renewed

1. All of the following were renewed for 1 year: Ad Hoc Task Force on Conflicts of Interest (June 1991); Ad Hoc Committee on Legislation Affecting Quality of Care (June 1991); Ad Hoc Committee on Liaison Activities (June 1991); Ad Hoc Committee to Plan for APA's Sesquicentennial (June 1991); Ad Hoc Committee for the Pilot Advocacy Project (June 1991).

Education

1. Authorized the Council on Medical Education and Career Development to further explore the feasibility of a policy that would require APA to sponsor programs (in addition to those at annual meetings and H&CP institutes) for members to help them prepare to take board examinations (Dec. 1991).

2. Affirmed that APA will follow the "Guidelines for Commercial Support of Continuing Medical Education," which recently were adopted by the Accreditation Council on Continuing Medical Education (Dec. 1991).

3. Voted to change APA's continuing medical education (CME) requirements to be consistent with recently revised AMA CME requirements (June 1991).

4. Postponed, until the March 1992 meeting of the Board, action on APA joint sponsorship of CME activities (Dec. 1991); further, deferred again any action regarding termination of APA joint sponsorship of CME activities, to enable further discussion with district branches (March 1992).

5. Accepted the report of the Task Force on Educational Activities for Diagnostic Systems (regarding the *DSM-III-R* Diagnostic Practice Survey) for appropriate use; further, voted to release the data to the authors of the report for their use in independently published articles (Dec. 1991).

6. Authorized the Task Force on Educational Activities for Diagnostic Systems to conduct a follow-up of an initial survey to collect data on psychiatrists' different cognitive styles and approaches to diagnosis in their use of *DSM-III-R* (Dec. 1991).

7. Authorized the Council on Medical Education and Career Development to convene a 1-day meeting consisting of six representatives (two each from APA, the ABPN, and the Residency Review Committee for Psychiatry) to address issues related to accreditation of subspecialty fellowship training programs and certification of individuals completing such programs (June 1991).

8. Voted to recommend to the Association of Directors of Medical Student Education Programs that each department of psychiatry identify a director of medical student education who will spend a significant portion of time addressing issues related to undergraduate medical education and recruitment of medical students into psychiatry; further, authorized the Council on Medical Education and Career Development to send a letter to the American Association of Chairmen of Departments of Psychiatry, enlisting the support of its members in addressing issues involving recruitment into psychiatry (Dec. 1991).

9. Voted to ask APA's representatives on the Residency Review Committee for Psychiatry to remind committee site visitors of issues involving compliance with the requirement for training in transcultural issues (Dec. 1991).

10. Approved the following slate of resident nominees to be considered for selection as resident representative by the Residency Review Committee for Psychiatry: Drs. Gerald Bunting Blake, Peter Della Bella, and David Hackney (March 1992).

11. Authorized the Committee on Residents and Fellows and the Council on Medical Education and Career Development, following established procedures and working in conjunction with the Medical

Director's office, to seek outside funding of approximately \$14,000 to support production and distribution of the *Psychiatric Residents' Newsletter* three times a year (June 1991).

12. Authorized the President or Medical Director to send a letter to the Residency Review Committee for Psychiatry, calling for an addition to the "Special Requirements for Residency Training in Psychiatry," stating that "programs must have a plan to foster the development of skills for those residents interested in conducting psychiatric research. This plan should include opportunities for conducting research under the supervision of a mentor and training in the principles and methods of research" (Dec. 1991).

13. Authorized the Medical Director to send letters to the American Association of Directors of Psychiatry Residency Training and the American Association of Chairmen of Departments of Psychiatry, asking for each organization's position on major issues related to subspecialty fellowship programs (Dec. 1991).

Elections

1. Authorized the results of the mail ballot in which the results of the 1991 election were accepted and the decision to dispose of the ballots was postponed until the Board meeting on May 12, 1991 (May 1991).

2. Authorized staff to destroy the ballots from the 1991 election immediately after the 1991 annual meeting (May 1991).

3. Accepted the results of the 1992 election and authorized staff to destroy the ballots from the election after the 1992 annual meeting (March 1992).

4. Changed the mailing date for the ballots from February 20 to February 5 and to approve appropriate changes to the "Operations Manual of the Board of Trustees" (June 1991).

5. Approved changes to section A.2.c. of "Election Procedures," in the operations manual appendix F-1, to read, "Biographies of candidates are limited to six items in seventy-five words (exactly)" (this is based on the word-counting method described in the report of the Elections Committee, using *Webster's Ninth New Collegiate Dictionary*, 1989 edition, as the standard) (June 1991).

6. Approved the addition of a paragraph (paragraph 3) to section II.E. of "Guidelines for Nomination and Elections," in the operations manual appendix F-2, and renumbering paragraphs II.E.3-7 as II.E.4-8; the new paragraph would end statements and answers to questions once the word count has been reached (June 1991).

7. Approved the addition of a paragraph (paragraph 4) to section II.A. of "Guidelines for Nomination and Elections," in operations manual appendix F-2, and renumbering paragraphs II.A.4-7 as II.A.5-8; the new paragraph would require candidates to include a summary of the guidelines in their letters to members who are asked to support them (June 1991).

8. Affirmed the policy that signatures on a petition are valid only for the year in which the petition is initially submitted and that petitioners are required to resubmit a new petition with the requisite number of current signatures if they wish the petition to be on the ballot in the next year's election (March 1992).

Ethics

1. Approved the following regarding the composition of the Ethics Appeals Board: a) the Secretary will continue to chair the Ethics Appeals Board, which will consist of five members (two past Presidents, a past Speaker of the Assembly, the chairperson of the Ethics Committee, and a chairperson of a district branch ethics committee); b) tenure for members will be extended to 3 years; c) members will be selected from those who have hands-on ethics committee experience at either the local or the national level and who are strongly committed to the ethics process (Sept. 1991).

2. Established an ad hoc committee, appointed on a 4-year cycle, to review the activities of the Ethics Appeals Board and to report to the Assembly and Board of Trustees (Sept. 1991).

3. Approved the policy that, at the time of an appeal, the appellant and his or her lawyer will be notified of the following four criteria for appeal and requested to answer a series of questions that identify which of the four criteria are being appealed: a) there have been procedural irregularities or deficiencies; b) *The Principles of Medical Eth-*

ics With Annotations Especially Applicable to Psychiatry have been improperly applied; c) there is no substantial evidence to justify the findings or sanction imposed by the district branch; or d) substantial new evidence brings into question the findings and conclusions of the district branch ethics committee (Sept. 1991).

Fiscal Issues

1. As reported out of executive session, voted to include funding (approximately \$3,000) in the 1992 APA budget for the Work Group on Model Standards for Private Long-Term Care Insurance (Dec. 1991).

2. Tentatively approved the \$25.4-million 1992 APA operating budget, noting that final approval of the budget would be given in December 1991 (Sept. 1991).

3. Approved the 1992 APA budget of approximately \$24.7 million, with the understanding that if the trend of declining revenue worsened during the year, additional reductions in the budget could be made (Dec. 1991).

4. Voted to ask the Treasurer, the chairperson of the Budget Committee, legal counsel, and a representative of APA's auditing firm to review current APA procedures for audit reporting to determine if there are any problems, concerns, or issues and to return to the Board with recommendations for any needed change (June 1991).

5. Authorized the execution of all documents necessary to implement fiscal transactions with American Security Bank, subject to approval of such documents by legal counsel (June 1991).

6. Established an account with First National Bank of Maryland, D.C. (March 1992).

7. Authorized deduction of \$3,000 from the budget allocation for managed care litigation and expenditure of this amount to support the newly formed Joint Assembly/Board Task Force to Review Medical Necessity and Reimbursement Criteria for Use by Managed Care Organizations and Payers of Psychiatric Care (June 1991).

8. Authorized use of the balance of unexpended monies in the 1991 Board of Trustees contingency fund (after all funds authorized for 1991 were spent as needed) as the Board contingency fund through the tenure of the current Board (May 1992); further, authorized making the 1992 Board contingency fund the 1992-1993 Board contingency fund (beginning with the tenure of the new Board), with the understanding that in the future the allocation of Board contingency fund monies would be synchronized with the tenure of the Board (i.e., from May to May) (Dec. 1991).

9. Authorized a member of the APA Consultation Service Board and another appropriate individual to make a short visit to Puerto Rico to clarify the nature of the assistance needed by Puerto Rico and to report to the Board of Trustees in May 1992; further, voted to allocate up to \$5,000 from the Board contingency fund to support this trip (March 1992).

10. Approved the 1992 membership dues structure, which incorporates a weighted aggregate increase of 4.4% (Sept. 1991).

11. Established a program whereby General Members or Fellows who are 40 or more years of age may pay a lump sum to the Association and shall not be required to pay further annual dues or assessments (to continue as members or Fellows of APA, such members must continue to meet all other requirements of membership, including ethical conduct and continuing medical education, and must remain members in good standing of a district branch of the Association; no refund of lump-sum dues payments shall be made for any reason, including death, disability, resignation, or expulsion from the Association) (June 1991).

12. Approved the amount of the required lump-sum dues payment through Dec. 31, 1991; further, authorized the option of making such a payment in two installments over a period not to exceed 15 months, provided that the member pays a 10% installment fee (10% of the second payment) (June 1991).

13. Voted to require staff and the Budget Committee to report annually to the Board of Trustees on the implementation of the lump-sum dues payment program, the number of members who have exercised this dues option, and the amounts from such lump-sum dues payments that are invested in the Continuing Dues Payment Fund and the Board Restricted Investment Fund (June 1991).

14. Authorized the Treasurer to establish a special fund, called the

Continuing Dues Payment Fund, into which a portion of each lump-sum dues payment shall be deposited at an amount to be determined by financial staff and from which, each year, an amount equal to the annual dues that the member would have paid will be transferred into the membership dues account (June 1991).

15. Authorized the Treasurer to establish a special fund to be called the Board Restricted Investment Fund, into which all receipts from lump-sum dues payments that are not deposited in the Continuing Dues Payment Fund shall be deposited (June 1991).

16. Authorized APA, after appropriate negotiation by the Medical Director, to accept \$150,000 per year for 3 years from Abbott Laboratories to support educational activities of the Association (June 1991).

17. With respect to financial planning, voted a) to establish a target for liquid reserves of 3 months of staff salaries; b) to request the chairperson of the Committee on Human Resources to attend meetings of the Budget Committee as a consultant; c) to terminate the Investment Advisory Committee with an expression of appreciation to its members for many years of valuable service; d) to require that all proposed capital expenditures be included in a capital budget submitted as part of the operating budget (Sept. 1991).

18. Authorized the Committee on History and Library, following established procedures and working in conjunction with the Medical Director's office, to seek outside funding (\$50,000-\$100,000) to construct a new rare books room within the APA Library (June 1991).

19. Authorized changing the line of mutual funds offered by the APA member retirement program to the Heritage line of mutual funds managed by Raymond James and Co. (June 1991).

20. Approved increasing the daily stipends for the President, President-Elect, Speaker, and Speaker-Elect to \$500/day or the proportionate amount per part day, to be applicable to all future billings (June 1991).

21. Approved changes to the plan document for the APA retirement savings plan (March 1992).

22. Authorized attempts to find continued funding for the State/University Collaboration Project and to consider establishing a presence or staff office within APA for this function (Dec. 1991).

23. Approved a new fiscal policy on member and staff travel reimbursement (Sept. 1991).

Forensic Psychiatry

1. Approved the "Position Statement on Peer Review of Expert Testimony" (approved by the Assembly in November 1991) but deferred action on the accompanying background document until the March 1992 Board meeting to permit concerned members of the Assembly to discuss it and offer further comments (Dec. 1991).

2. Accepted the revised resource document on peer review of expert testimony accompanying the "Position Statement on Peer Review of Expert Testimony," which was approved by the Assembly and the Board in November and December 1991, respectively (March 1992).

3. Approved the revised "Report of the Task Force on the Use and Misuse of Psychiatric Diagnoses in the Courts" for publication as an APA task force report (Dec. 1991).

4. Endorsed, as a resource document, "Right to Refuse Medication: Judicial Review Supplement" (Dec. 1991).

Governance

1. Approved the recommendation of the Committee on Constitution and Bylaws to approve an amendment to chapter 8.5 of the Bylaws for reading to the membership at the 1992 annual meeting and placement on the 1993 ballot; the amendment would ensure that a referendum which passes would have a majority of the votes (March 1992).

2. Referred to the Committee on Constitution and Bylaws a recommendation that the Bylaws be amended to permit reporting to the membership and the National Practitioners Data Bank the name of any member against whom an ethics complaint is filed within 90 days of his or her resignation (wording for the amendment approved by an Executive Action in April 1992 and scheduled for ratification at the May Board meeting) (March 1992).

3. Approved new procedures for implementing APA conflict of interest policy (March 1992).

4. Voted to distribute to the district branch and state association presidents the document "Fiduciary Responsibilities of Association Officers and Board of Trustees Members"; further, voted to use this document in the training of new officers, Board members, Assembly representatives, and district branch presidents-elect (Dec. 1991).

5. As reported out of executive session, was informed that the law firm of Onek, Klein, and Farr would become Klein, Farr, Smith, and Taranto as of June 28, 1991, and that senior partners Mr. Joe Onek and Ms. JoAnn Macbeth would be moving to the firm of Crowell and Moring; it was anticipated that Mr. Joel Klein could continue to provide services to APA through December 1991, and a small advisory committee of Drs. John McIntyre, Elissa Benedek, and Carolyn Robinowitz was appointed to discuss issues related to future APA legal representation (June 1991).

6. Voted to retain Ms. JoAnn Macbeth of the firm Crowell and Moring as general counsel and to authorize the Medical Director to enter into contract/fiscal negotiations with Ms. Macbeth and her firm for their services, reporting back to the Board in June (March 1992).

7. Approved specific arrangements for contracts with the editors of the three major APA periodicals, *American Journal of Psychiatry*, *Hospital and Community Psychiatry*, and *Psychiatric News*, including a 3-year contract for any new editor and, on the basis of a positive performance evaluation, renewal for two 5-year periods, with the understanding that each editor should serve no longer than 13 years as editor of one of these three periodicals (March 1992).

8. Authorized the Medical Director and the President to establish a component that will begin to develop evaluation criteria for the editors of the three major APA periodicals (March 1992).

9. Authorized Drs. Hartmann and English to implement a May 1988 action of the Board (i.e., to review and evaluate each editor of the major APA periodicals who is appointed by the Board of Trustees, in the third year of editorship and every 5 years thereafter) and then to return to the Board in June with a recommendation about offering contracts (renewable or not) to the existing editors (March 1992).

10. Approved the "Conflict of Interest" policy for inclusion in the APA personnel manual, with the understanding that the final version would be approved by general counsel (Dec. 1991).

11. Approved the "Code of Ethics" policy (subject to final approval by general counsel) for inclusion in the APA personnel manual (Dec. 1991).

12. Approved the "Drug-Free Workplace" policy (subject to final approval by general counsel) for inclusion in the APA personnel manual (Dec. 1991).

13. Approved the "Sexual Harassment" policy (subject to final approval by general counsel) for inclusion in the APA personnel manual (Dec. 1991).

14. Waived current policy to permit Dr. Kenneth Paul Rosenberg to be reappointed to serve an additional year (through May 1993) as a member and chairperson of the Subcommittee on Video of the Scientific Program Committee (Dec. 1991).

15. Waived the policy in the operations manual to permit reappointment of Dr. Jeremy Lazarus as member and chairperson of the Ethics Committee for 1 additional year (through May 1993) (March 1992).

16. Recommended to the Budget Committee that it continue support of efforts to resolve the member/manpower shortage of the Scientific Program Committee (June 1991).

17. Requested the Medical Director to search promptly for psychiatrists to direct APA's Office of National/Minority Affairs and Office of Education, asking him to report progress to the Board in December 1991 (Sept. 1991).

Government Relations

1. Voted not to support the reorganization of ADAMHA at this time, until APA has consulted with other constituency groups and until issuance of the forthcoming Institute of Medicine report on the federal government's organization for administering research and services (June 1991).

2. Voted "that APA continues to have serious reservations about the proposal to reorganize ADAMHA and that APA will work to

ensure that any outcome is in the best interests of the mentally ill of this country" (Sept. 1991).

3. Authorized APA's support of efforts at both the state and federal levels to ensure that adequate funding is made available for clozapine treatment and for appropriate monitoring of all patients for whom this medication is likely to be of significant benefit (Dec. 1991).

4. Authorized legal counsel to prepare an opinion on the legal aspects and feasibility of APA's challenging recent interpretations reported in the *Federal Register* that would forbid psychiatrists to code for hospital admission and individual psychotherapy on the same day (Dec. 1991).

5. Voted to support the HealthAmerica Act (S. 1227) introduced jointly by Senators George Mitchell (D-Maine), Edward Kennedy (D-Mass.), Jay Rockefeller (D-W.Va.), and Donald Riegle (D-Mich.) on June 5, 1991 (June 1991).

6. Reaffirmed its policy of urging state legislators and regulators to adopt the requirement that hospital admissions be limited to psychiatrists who adhere to the following criteria: a) every admission, voluntary or involuntary, must be clinically justified by the admitting psychiatrist; b) each patient admitted by a psychiatrist may be admitted only after he or she is evaluated face-to-face by the admitting psychiatrist who determines the necessity of the admission; and c) in an emergency, the admitting psychiatrist may order by telephone whatever measures are needed for the safety of the patient (the face-to-face evaluation should occur as soon as possible but no longer than 6 hours after an emergency admission) (this emergency provision excludes children under age 14, each of whom must be seen by a psychiatrist before admission) (March 1992).

7. Endorsed a joint public affairs/legislative affairs campaign to enact state legislation to regulate managed care in states that have not acted on such legislation (using a draft model state bill developed by the Joint Commission on Government Relations and the Division of Government Relations) (March 1992).

8. Authorized the Division of Government Relations, working with ADAMHA, the National Institutes of Health, and Congress, to advocate for a loan forgiveness program for individuals engaging in psychiatric research training programs (Dec. 1991).

9. Voted to support the Medical Substance Abuse Treatment Act of 1991, recognizing that treatment services should be covered in all appropriate settings under medical supervision (in addition to residential settings) (Dec. 1991).

10. Endorsed the "Statement on Vocational Rehabilitation for Persons With Disabilities" developed by the National Task Force on Rehabilitation and Employment of Persons with Psychiatric Disabilities, with the understanding that additional comments from the APA Committee on Disability and Rehabilitation would be forwarded to the national task force (March 1992).

11. Authorized APA to work for additional federal funding to support the Women and Alcohol Research Equity Act (June 1991).

Homelessness

1. Approved the report of the Task Force on the Homeless Mentally Ill for publication as a task force report (Dec. 1991).

Hospital and Community Psychiatry Journal

1. Approved the reappointment of Dr. Leonard Stein and the appointment of Drs. Jeffrey L. Geller and George M. Simpson to the H&CP Editorial Board (March 1992).

Hospitalization

1. Approved a resolution to support the following guidelines for psychiatrists who admit patients to hospitals: a) every admission, voluntary or involuntary, must be clinically justified by the admitting psychiatrist; b) each patient admitted by a psychiatrist may be admitted only after he or she is evaluated face-to-face by the admitting psychiatrist who determines the necessity of the admission; and c) in an emergency, the admitting psychiatrist may order by telephone whatever measures are needed for the safety of the patient (the face-to-face evaluation should occur as soon as possible but no longer than 6 hours after an emergency admission) (this emergency provision ex-

cludes children under age 14, each of whom must be seen by a psychiatrist before admission) (March 1992).

Institute on Hospital and Community Psychiatry

1. Authorized the Committee on Universal Access to Health Care to seek outside funding, following established procedures and working in conjunction with the Medical Director's office, to support travel expenses for speakers and discussants at the half-day workshop on universal access at the 1992 H&CP institute (March 1992).

2. Extended the application of the revised guidelines for pharmaceutical or other industry-sponsored symposia to the Institute on Hospital and Community Psychiatry, beginning with the 1992 institute; further, voted that all requests for revisions to the guidelines must be referred to the Committee on Advertisers and Exhibitors and be made in conjunction with the program committees for both the annual meeting and the institute (Sept. 1991).

3. Voted to suspend (commencing with the 1992 annual meeting) the solicitation and display of scientific exhibits at annual meetings and H&CP institutes (Sept. 1991).

4. Approved the following policy for selection of APA meeting sites: APA will consider any significant conflict between a state's laws or policies and corresponding policies/positions of APA, and APA's policy positions will be weighed in making these decisions; further, agreed that if APA decides to meet in a restrictive state (e.g., anti-choice), APA will consider constructive ways to educate the public and to advocate for APA's position during the meeting (June 1991).

Insurance Programs

1. Asked Mr. Joel Klein, APA legal counsel, Mr. Rich Feeley, APA insurance and financial consultant, Dr. Sabshin, and Dr. Robinowitz to prepare clearly worded options for any changes recommended in APA's policy of indemnification of district branch activities, with the understanding that APA currently indemnifies the district branches only for activities related to ethics (June 1991).

It was recommended that APA assume the deductible under its directors and officers insurance policy in claims against district branches and state societies, otherwise covered by insurance, arising out of a) actions affecting membership status or b) other actions or activities undertaken by the district branch or state society at the written request or direction of APA. After discussion, the Board voted to postpone consideration of this item until its December meeting, requesting the Budget Committee to prepare a financial impact statement (Sept. 1991).

2. Postponed until March 1992 any action and further discussion on the plan for extending APA's coverage of the cost of the deductible in the directors and officers insurance plan for district branches and state associations, with the understanding that the proposal (including fiscal implications and exactly what the Association would be covering) would be presented to the Board in writing (Dec. 1991).

3. Voted to assume the deductible under the APA directors and officers insurance policy in claims against district branches and state societies, otherwise covered by insurance, arising out of a) actions affecting membership status or b) other actions or activities undertaken by the district branch or state society at the written request or direction of APA (March 1992).

4. Approved a plan for cost sharing between APA and the district branches to cover the deductible of the directors and officers liability insurance in cases that are not covered by any other arrangement; the formula for this coverage is as follows: the district branch will assume \$2,000 plus \$40 per full-dues-paying member and a prorated amount for all other dues-paying members, based on their dues rates, and APA will assume the balance (March 1992).

5. Approved settlement in the lawsuit *Insurance Equities Corporation v. APA*, as recommended by legal counsel; further, authorized any officer of APA to execute the settlement agreement (Dec. 1991).

International Affairs

1. Authorized sending letters to the medical officers of health in the countries in the new Commonwealth of Independent States (former Soviet Union), indicating APA's appreciation of the extreme difficulties being faced, expressing APA's concern that the mentally ill are at

great risk of deprivation in hard times, asking the officials to ensure that supplies of food and medicine are provided to all psychiatric hospitals, and insisting that the victims of psychiatric abuses under the former Communist regime continue to receive the rehabilitation they require (March 1992).

2. Authorized sending a letter to the director of the Serbsky Psychiatric Institute in Moscow, urging her to express public concern about the use of confidential psychiatric records to denounce political figures and, moreover, the use of such records for any purpose not related to the subjects' best interests (March 1992).

3. Authorized the Committee on International Education to organize a series of roundtable symposia in Central and South America to discuss psychiatric educational curricula; authorized the committee to seek cosponsorship with the InterAmerican Council of Psychiatric Organizations; and authorized the committee to seek outside funding, following established procedures and working in conjunction with the Medical Director's office, to support this project (Dec. 1991).

4. Authorized the Committee on International Education to gather data and to produce an international directory of psychiatry, in conjunction with the Committee of Hispanic Psychiatrists, Committee of Asian-American Psychiatrists, and Committee on International Medical Graduates and with the AMA, the Educational Commission on Foreign Medical Graduates, and the Pan American Health Organization; further, authorized the committee to seek outside funding, following established procedures and working in conjunction with the Medical Director's office, to support the development of this directory (Dec. 1991).

5. Approved printing on APA stationery a form to be used as an official APA document for investigating human rights abuses and abuse/misuse of psychiatry (Dec. 1991).

6. Approved printing the document "Human Rights and the APA" in booklet form for distribution to interested members and parties in other countries (March 1992).

7. Voted to request executives of the World Psychiatric Association (WPA) to advise the All Union Society of Psychologists and Narcologists of the U.S.S.R. that their conditional membership will be revoked if the criteria for readmission are not fully met; further, voted to strongly urge the WPA to provide the necessary funding to support the requisite site visit (June 1991).

8. Approved statements recommending that the WPA revoke the membership of the All Union Society of Psychiatry and Narcologists of the U.S.S.R. for failing to adequately fulfill the conditions placed on the restoration of membership by the WPA General Assembly in October 1989 and that the WPA (in the light of recent political developments in the Soviet Union) be prepared to expand its contacts with Soviet psychiatry by recognizing recently established and newly emerging psychiatric associations as they fulfill the standards and requirements of the WPA (Sept. 1991).

9. Authorized APA cosponsorship of a joint Soviet-American conference on ethical issues in psychiatry with the Georgetown-Johns Hopkins Program in Law, Ethics, and Health, the Program in Medical Ethics of the University of Wisconsin School of Medicine, and the Schell Center on International Human Rights; further, authorized the Council on International Affairs, following established procedures and working in conjunction with the Medical Director's office, to seek outside funding to cover the costs of the conference (June 1991).

Judicial Activities

1. Ratified an Executive Action taken by the President, the Speaker, and Dr. Carolyn Robinowitz, Acting Medical Director, authorizing APA to sign onto a brief prepared by the American College of Obstetricians and Gynecologists and filed in the Supreme Court case *Planned Parenthood of Southeastern Pennsylvania v. Robert P. Casey* (March 1992).

2. Ratified an Executive Action taken by the President, the Speaker, and Dr. Carolyn Robinowitz, Acting Medical Director, authorizing APA to sign onto a brief prepared by the National Alliance for the Mentally Ill and filed in the U.S. Court of Appeals for the Second Circuit in the case *Disabled American Veterans v. U.S. Department of Veterans Affairs* (also signing onto the brief were the Mental Health Law Project and the National Mental Health Association) (March 1992).

3. Authorized APA to file an amicus curiae brief with the U.S. Supreme Court in *Foucha v. Louisiana*, a case involving the question of whether defendants acquitted on the basis of the insanity defense may be kept hospitalized, once they are no longer mentally ill, solely on the grounds of dangerousness (May 1991).

4. Authorized APA to file an amicus curiae brief in the Second Circuit Court of Appeals in the case *U.S. v. Steven Diamond* (Sept. 1991).

5. Ratified the Executive Action taken by the President, Speaker, and Medical Director authorizing APA to file an amicus brief in the Supreme Court in support of the petitioner in *Riggins v. Nevada* (Dec. 1991).

Liaison Activities

1. Authorized APA to participate, at no cost to APA, in a joint APA and American Bar Association work group (under the aegis of the Council on Children, Adolescents, and Their Families) addressing the problems of children damaged by the divorce process and the adversarial system; further, authorized a liaison with the American Bar Association through the council for the narrow and express purpose of assisting with the proposed study (approximately 2 years) (Sept. 1991).

2. Approved APA cosponsorship of the Behavioral Healthcare Symposium to be held Sept. 9–12, 1992, in Chicago (Dec. 1991).

3. Authorized APA to develop guidelines for psychiatrists working in public and private organized systems of care; further, authorized APA to work with the National Association of Private Psychiatric Hospitals in its revision of guidelines (Dec. 1991).

4. Voted to send a clear message to the board of the National Association of Private Psychiatric Hospitals that APA does not support its admission standards and that APA questions its definition of a psychiatrist (Dec. 1991).

5. Approved a resolution to support the following guidelines for psychiatrists who admit patients to hospitals: a) every admission, voluntary or involuntary, must be clinically justified by the admitting psychiatrist; b) each patient admitted by a psychiatrist may be admitted only after he or she is evaluated face-to-face by the admitting psychiatrist who determines the necessity of the admission; and c) in an emergency, the admitting psychiatrist may order by telephone whatever measures are needed for the safety of the patient (the face-to-face evaluation should occur as soon as possible but no longer than 6 hours after an emergency admission) (this emergency provision excludes children under age 14, each of whom must be seen by a psychiatrist before admission) (March 1992).

6. Approved APA's becoming an organizational member of the Liaison With the National Coalition on Alcohol and Other Drug Issues, at no cost to APA (Dec. 1991).

7. Authorized APA to give high priority to efforts to have a psychiatrist appointed to the National Committee on Vital and Health Statistics (Dec. 1991).

8. Approved APA's participation with the National Foundation for Depressive Illness, Inc., to develop a program for educating generalists about affective disorders (Sept. 1991).

9. Approved APA cosponsorship of the 1992 National Mental Health Association Scientific Symposium, to be held Aug. 9–11, 1992, in Charleston, S.C. (March 1992).

10. Authorized continued liaison with the Rehabilitation Services Administration through the Council on Psychiatric Services and payment of travel expenses from the budget of the Council on Psychiatric Services (June 1991).

11. Authorized the President to select nominees that can be recommended to the Utilization Review Accreditation Committee board of directors to serve on committees that will be developing standards and accreditation procedures, with the understanding that APA would bear the travel costs of such representatives (June 1991).

Managed Care

1. Voted to return the \$26,535 given by the Connecticut Psychiatric Society to APA to support litigation in the managed care industry with a strong expression of APA's appreciation (plus the interest that accrued in the escrow account) (Dec. 1991).

2. Adopted the strategic groupings and priorities for addressing managed care issues as listed in the "Report of the Assembly Ad Hoc Task Force on Managed Care" and referred the report to the Committee on Managed Care, requesting that it report back to the Board, and thanked the Assembly for its major efforts and hard work (Dec. 1991).

3. Created the four-member joint Assembly and Board Task Force to Review Medical Necessity and Reimbursement Criteria for Use by Managed Care Organizations and Payers of Psychiatric Care, to provide consultation to the General Electric Corporation and to respond to subsequent requests from other organizations; further, allocated \$3,000 from the Board of Trustees contingency fund to support start-up costs of this component (June 1991).

4. Adopted guidelines to be considered whenever APA provides criteria review for the managed care industry (Dec. 1991).

5. Approved the policy that APA will not endorse externally developed utilization review criteria and voted that this policy should be made known to parties seeking endorsement or review and that no promise of review should be given when parties inquire about review; further, voted that the triage mechanism for incoming criteria be implemented (i.e., that an executive committee, consisting of the chairpersons of the Council on Economic Affairs and the Committee on Quality Assurance plus a deputy medical director, review the incoming criteria to decide APA's interest in pursuing them further) (Sept. 1991).

6. Authorized APA to develop guidelines for psychiatrists working in public and private organized systems of care (Dec. 1991).

7. Endorsed publication of "Utilization Management: A Handbook for Psychiatrists" as a task force report, contingent on a positive response from the Assembly Executive Committee (within 1 week or 10 days), noting that if a conflict emerges, the Executive Action mechanism will be used to decide whether to publish this document (Sept. 1991).

8. Ratified an Executive Action taken by the President, Speaker, and Medical Director to approve publication and wide distribution of "Utilization Management: A Handbook for Psychiatrists" (Dec. 1991).

Membership

1. Approved advancement of 179 General Members to Fellow status; approved advancement of three Life Members to Life Fellow status; and deferred advancement of 41 General Members to Fellow status (names on file) (Dec. 1991).

2. Approved 31 applications for Corresponding Membership; approved six nominations for new Corresponding Fellows; and approved the advancement of one Corresponding Member to Corresponding Fellow (names on file) (Dec. 1991).

3. Authorized holding a feasibility meeting in early 1992 to allow an in-depth exploration of membership directory issues by selected members of the Committee on Membership, the chairperson of the Committee on Biographical Directory and Research on Psychiatric Professional Activities, and APA staff (as assigned by the Senior Deputy Medical Director, Dr. Robinowitz) (Dec. 1991).

4. Authorized the Committee on Membership to produce a limited membership directory by 1994, creating a subcommittee on this project; further, authorized the Committee on Membership to develop a budget and to seek outside funding, following established procedures and working in conjunction with the Medical Director's office, to support this project (March 1992).

5. Approved dues relief and/or transfer to Inactive status for 323 members; denied dues relief and/or transfer to Inactive status for 32 members; and approved 37 requests for dues relief and/or transfer to Inactive status pending district branch recommendations (names on file) (Dec. 1991).

6. Encouraged members who were called to active duty for Operation Desert Shield and/or Desert Storm to apply for dues relief if needed; further, voted to request that such an announcement be published in an upcoming issue of *Psychiatric News* (June 1991).

7. Voted to expel Dr. Pradeep B. Kakkad from APA and the Illinois Psychiatric Society for noncompliance with conditions imposed on him as a suspended member (as a past chairperson of the Ethics Committee, Dr. McDevitt abstained from the vote) (June 1991).

8. Voted to expel Dr. Sergio Toscano from APA for violation of section 1, annotation 1, and section 2, annotation 2, of the *Principles of Medical Ethics With Annotations Especially Applicable to Psychiatry*; further, voted to request that the Ethics Committee approve reporting the expulsion of Dr. Toscano to the Mexican Psychiatric Association (Dec. 1991).

9. Approved the nominations of Jean Endicott, Ph.D., Patricia van Ameringen Kind, Ph.D., and Rachel Gittelman Klein, Ph.D., for Honorary Fellowship in APA; further, voted to elevate Leo E. Hollister, M.D., from Associate Member to Distinguished Fellow (Dec. 1991).

10. Authorized a market research study on membership services; approved funding from the 1992 budget (not to exceed \$20,000) for the portion of this study not funded by other entities; and authorized the work of the Ad Hoc Work Group to Advise the Membership Committee on Membership Losses to continue through the completion of this project and to include oversight of the marketing studies and coordination of input from the involved entities (Dec. 1991).

11. Endorsed actions taken by the Assembly regarding meeting the needs of military psychiatrists eligible for APA membership who are on active military duty (Dec. 1991).

12. Voted to change the "Operations Manual of the Board of Trustees" to include language that would permit the use of proof of acceptance to sit for examination by either the ABPN or the Royal College of Physicians and Surgeons of Canada as a method of demonstrating eligibility for APA General Membership for psychiatrists who received psychiatric training abroad, with the understanding that Dr. Aron Wolf, chairperson of the Committee on Membership, would consult with Dr. Munoz on the final wording (Dec. 1991).

13. Voted to deny an application for General Membership submitted by the Oklahoma Psychiatric Association because the applicant did not fulfill the requirement of completion of a psychiatry residency training program approved by the Accreditation Council for Graduate Medical Education (ACGME) (name on file) (June 1991).

14. Voted to deny applications for General Membership submitted by the Massachusetts Psychiatric Society and the Quebec and Eastern Canada District Branch (two applications apiece) because none of the applicants fulfilled the requirement of completion of an ACGME-approved psychiatry residency training program (names on file) (June 1991).

15. Denied membership to an applicant for Member-in-Training from the Iowa Psychiatric Society who is receiving psychiatric training from a residency training program approved by the American Osteopathic Association, unless he enters an ACGME-approved program (name on file) (Dec. 1991).

16. Deferred two applications from the Massachusetts Psychiatric Society, one from an applicant who does not meet the requirements for General Membership and one from an applicant who is attending a training program not approved by the ACGME and therefore does not meet the requirements for Member-in-Training status (names on file) (Dec. 1991).

17. Approved an application from the New Jersey Psychiatric Association for General Membership (name on file) (Dec. 1991).

18. Voted not to change the membership enrollment date of a Member-in-Training whose application through the Northern California Psychiatric Society took 18 months to process (name on file) (Dec. 1991).

19. Voted to drop from membership 562 members whose dues were in arrears for 1990 (names on file); further, recommended that administrative reinstatement be authorized for those who returned to good standing by Sept. 14, 1991, and were also in good standing in their district branches (June 1991).

20. Authorized dropping from APA membership as of Oct. 1, 1991, seven members who were in arrears for 1990 APA dues (names on file); further, authorized administrative reinstatement of those who returned to good standing in APA and were in good standing in their district branches by Nov. 1, 1991 (Sept. 1991).

21. Authorized dropping from APA membership 17 members who were in arrears for 1990 APA dues (names on file) (Dec. 1991).

22. Authorized dropping 118 Medical Student Members who had graduated from medical school unless they submitted appropriate documentation to enable them to advance to Member-in-Training status (names on file) (Dec. 1991).

23. Authorized dropping from APA membership as of March 1992

a member who failed to meet the membership requirement of completion of an ACGME-approved residency training program (name on file) (March 1992).

24. Voted to drop from APA membership 230 members who had been dropped by or had resigned from their district branches (names on file); further, authorized administrative reinstatement of those who returned to good standing in their district branches and were also in good standing in APA (June 1991, Sept. 1991, Dec. 1991, March 1992).

Minority Activities

1. Voted to release to the authors the monograph "Ethnic Differences: Do You Amend Your Therapeutic Approach?" for independent publication, provided that references to APA were removed (Dec. 1991).

2. Approved the position statement on homosexuality and the U.S. Immigration and Naturalization Service (4) (June 1991).

3. Authorized the Committee on International Medical Graduates, following established procedures and working in conjunction with the Medical Director's office, to seek outside funding (approximately \$8,000) to produce and distribute a newsletter for international medical graduates (three issues per year with a circulation of 8,000) (June 1991).

4. Authorized the Committee on International Medical Graduates to seek approximately \$6,000 in outside funding, following established procedures and working in conjunction with the Medical Director's office, to support publication of proceedings of the last two international medical graduate regional meetings, with the understanding that the publications would not carry the imprimatur of APA (Dec. 1991).

National Issues

1. Approved the position statement on reproductive rights (5), contingent on the approval of the Assembly (which approved it in November 1991) (Sept. 1991).

2. Voted to release to the authors the series of papers concerning nuclear issues and military economy that were presented during the symposium "Psychosocial Dynamics of Big Defense Spending," sponsored by the Committee on Psychological Aspects of Nuclear Issues, at the 1990 annual meeting, with the understanding that APA's name would not be associated with the documents (June 1991).

3. Approved the following position statement on the right to privacy: "Be it resolved that the American Psychiatric Association supports the right to privacy in matters such as birth control, reproductive choice, and adult consensual sexual relations conducted in private, and supports legislative, judicial and regulatory efforts to protect and guarantee this right" (Dec. 1991).

4. Authorized the Committee on Telemedical Services, following established procedures and working in conjunction with the Medical Director's office, to seek outside funding (up to \$5,000) to support an exhibit and workshop to be held during the 1992 annual meeting (Sept. 1991).

5. Approved Area VI Action Paper 1, "Nondiscriminatory Coverage of Potentially Disabling or Life Threatening Mental Disorders," as approved by the Assembly in November 1991, assigning the responsibilities for the study to the Committee on Universal Access to Health Care, with authorization for two additional members of the committee and additional funding as approved in the 1992 budget (Dec. 1991).

Public Psychiatry

1. Authorized the Council on Psychiatric Services to invite the chairpersons of the Committee on Veterans' Affairs, the Committee on Psychiatric Services in Jails and Prisons, the Committee on Psychiatric Services in the Military, and the Committee on Psychiatric Services for Mentally Retarded and Developmentally Disabled Persons and a representative from the Assembly Committee of Representatives of Minority/Underrepresented Groups to join the consortium; further, authorized the Council on Psychiatric Services to review requests for representation and, subsequently, to directly invite

groups to join the consortium as the council sees appropriate (Dec. 1991).

2. Voted to request that the *Psychiatric News* Editorial Board consider a request from the Assembly Committee on Community Psychiatry to incorporate information from the public psychiatry network newsletter as a regular feature in *Psychiatric News* (Dec. 1991).

3. Approved the following recommendations regarding services in public mental health programs: a) a consideration in the review of a nominee for Fellowship in APA shall be work experience or contribution of time in a public mental health program; b) psychiatrists should be encouraged to work in or volunteer some time in public mental health programs; c) in the next biographical survey the amount of time each psychiatrist works in or volunteers in a public mental health program should be clearly quantified; d) APA and district branches should develop mechanisms to recognize those who provide or volunteer for direct services to the severely mentally ill; e) APA should encourage public mental health programs to develop ways in which psychiatrists may volunteer or provide services, teaching, supervision, or advocacy (June 1991).

4. Authorized the next biographical survey (or the next appropriate sample survey) to include clear categories to capture and differentiate the amount of time psychiatrists spend in various public psychiatric services (e.g., uncompensated care, care for the severely mentally ill, volunteer or paid services in public psychiatry agencies) (Dec. 1991).

5. Approved the following statement regarding rehabilitation services: "Psychiatric diagnosis and treatment should be promoted as an essential component of any rehabilitation program for severely mentally ill persons" (June 1991).

6. Approved the following statement regarding nondiscriminatory coverage for severely mentally ill persons: "Severely mentally ill persons should have access to and reimbursement for care equal to that of other psychiatric and medical patients" (June 1991).

7. Authorized APA to negotiate with pharmaceutical companies to sponsor opportunities for public psychiatrists to broaden their knowledge base, upgrade their technology, and achieve some respite from their demanding jobs through a recognition program (e.g., a fellowship in an academic center, a traveling or visiting scholar award, a research sabbatical, or an exchange of an academic psychiatrist with a public psychiatrist) (Dec. 1991).

8. Adopted the model job description for medical/clinical director in state mental health authorities (Dec. 1991).

Research

1. Approved establishing a subcomponent of the Committee on Research on Psychiatric Treatments, within the Council on Research, to develop a report on antidepressants and suicide, using existing council and committee funds (Sept. 1991).

2. Approved several resolutions to assist district branches in their efforts to refute attacks against ECT (June 1991).

3. Authorized APA to accept a professional services contract (approximately \$25,000) from the ADAMHA Office for Science for analysis of APA Faculty Survey data (Sept. 1991).

4. Authorized APA to accept funding (approximately \$7,000) from NIMH to pay for the printing of extra copies of *Psychiatric Research Report* for Members-in-Training (Sept. 1991).

5. Authorized APA to accept a professional services contract (approximately \$25,000) from NIMH for analysis of APA Professional Activities Survey data (Sept. 1991).

6. Authorized APA to accept a professional services contract (approximately \$25,000) from the National Institute on Drug Abuse for analysis of APA Professional Activities Survey data (Sept. 1991).

7. Authorized APA to accept professional services contracts (approximately \$25,000 each) from NIMH for data analysis related to research training (Sept. 1991).

Subspecialization

1. Approved APA's endorsement of added qualifications in forensic psychiatry and voted to notify the ABPN of APA's endorsement (June 1991).

Youth

1. Approved the document "Disclosure of Psychiatric Treatment Records in Child Custody Disputes" for publication as a report from the Task Force on Disclosure of Psychiatric Records in Child Custody Disputes, incorporating word changes prepared by Drs. Wiener and Zonana (June 1991).

2. Approved the "Position Statement on Day Care for Preschool Children" (6) and extended the tenure of the Task Force on Day Care for Early Pre-School Children until December 1993, to permit monitoring of day care legislation (Dec. 1991).

REFERENCES

1. Position statement on the care of pregnant and newly delivered women addicts (official actions). *Am J Psychiatry* 1992; 149:724
2. AIDS policy: guidelines for inpatient psychiatric units (official actions). *Am J Psychiatry* 1992; 149:722
3. AIDS policy: guidelines for outpatient psychiatric services (official actions). *Am J Psychiatry* 1992; 149:721
4. Position statement: homosexuality and the Immigration and Naturalization Service (official actions). *Am J Psychiatry* 1991; 148:1625
5. APA actions on reproductive rights (official actions). *Am J Psychiatry* 1992; 149:723
6. Position statement on day care for preschool children (official actions). *Am J Psychiatry* 1992; 149:586

Report of the Treasurer

Mary Jane England, M.D.

EXECUTIVE SUMMARY

Economic pressures on APA fiscal operations

U.S. economy continues in recession.

APA business cycle hits low point.

Results of 1991 financial operations

Revenue of \$24,263,081 received.

Expenses held to \$24,136,307.

Membership

Membership increased by net of 361 members during 1991—to total of 37,279 members.

Dues tied to inflation—resulting in 4.4% increase for 1992.

Lump-sum dues option chosen by 60 members.

Ballot initiative passed, approving reduced dues for Life Members/Fellows (elected effective 1993).

Member-in-Training dues restructured.

Debt management

APA borrowing for cash flow held to \$2.8 million.

APA obtains loans with favorable terms ($\frac{1}{2}\%$ over prime rate).

Association maintains record of repaying all loans in full and on time.

Strategic financial planning

Board of Trustees established Financial Planning Subcommittee of the Budget Committee in March 1991.

Goal of \$1.8 million (3 months' payroll) set for liquid reserve to reduce reliance on borrowing.

APA auditors reported sound financial statements, accounting system, and budget process.

Plans set in place to smooth out APA business cycle.

Procedure for review of total employee compensation (salaries and fringe benefits) implemented.

Vehicle for oversight of investments refined.

Operations streamlined through reorganization and automation.

Capital budget implemented.

Potential programs identified to increase nondues revenue.

Budget Committee acts as catalyst in development and prioritization of APA mission and goals.

the amount that APA will need to draw on its line of credit. This is a small step toward the high-priority financial goal of debt reduction through the establishment of liquid reserves.

In March 1992 representatives of APA's independent accounting firm, McGladrey & Pullen, presented a detailed report to the Board of Trustees on the results of their audit of APA's 1991 financial operations.

SERVICES FOR MEMBERS

Just as APA's most important resource is its members, its most important function is service to members and their patients. As of Jan. 1, 1992, total APA membership stood at 37,279. The Association realized a net gain of 361 members during 1991, which contrasts sharply with an average net gain of over 1,000 members per year during the 1980s. This plateauing of membership growth is projected to continue for the foreseeable future, primarily because the number of new members is expected to remain relatively stable.

Another membership trend is pertinent to this Treasurer's report; i.e., while the number of dues-paying members increased by 0.25% during 1991, the number of non-dues-paying members increased by over 5%. These figures for 1991 are actually part of a trend over the past several years showing a decrease of dues-paying members compared to an increase of non-dues-paying members.

The Association is making progress in offsetting the fiscal effects of this trend. First, 60 members have selected the recently available option of paying APA dues in a lump sum. This program has led to receipts totaling approximately \$400,000 to date. Second, approval was given to a constitutional amendment included in the 1992 ballot that permits charging newly elected Life Members/Fellows (elected effective 1993 and beyond) reduced dues rates for 10 years after conversion to Life status, whereas Life Members/Fellows have paid no dues in the past. Third, beginning in July 1991, a \$40 communications fee was approved for Life Members/Fellows who wish subscriptions to the *American Journal of Psychiatry*, formerly a perquisite of membership. Life Members/Fellows who will now pay limited dues will continue to receive the *American Journal of Psychiatry* at no charge.

At the same time, the Association has taken steps in response to the financial implications of another trend within its membership, namely, the growing population of Members-in-Training. APA has instituted a seven-step dues structure to reduce the dues burden of members who have recently completed residency and have just begun practice.

The Association strives to keep in step with the needs of its members. APA growth during the 1980s represented a response to growing member needs during that period. As plans were developed for fiscal year 1991, the leadership heard a clear message from members regarding their changing financial picture. The Association's response was also clear. Growth has been replaced by a hold-the-line budget. Dues increases beyond inflation, which helped to support the 10-year growth, have been replaced by dues rates tied to the rate of inflation. The dues increase for 1992 was 4.4%.

As an APA member you need to know that the Association focuses heavily on your needs, your problems, and your priorities. Only through your professional association can many of the needs that you face be addressed—and only through your communication of those needs can your views help shape APA's priorities.

RESPONSE TO ECONOMIC PRESSURES

In 1991 American corporations continued to post reductions in the scope of operations, level of output, and profits—while individual

GENERAL

This report is prepared from audited figures for the fiscal year that ended Dec. 31, 1991. The data presented also appear in the auditor's annual report.

Table 1 is a statement of our financial condition, taken from the independent auditor's report, and table 2 reflects functional revenues and costs. These will provide the membership with information needed to assess the operations and financial condition of the Association.

SUMMARY OF FISCAL RESULTS OF 1991 OPERATIONS

APA implemented a break-even budget for 1991 despite substantial obstacles posed by the national economy. Actual revenues of \$24,263,081 were below budget estimates by \$134,522, or about 0.5%. A shortfall in revenue had been anticipated early in the year, which prompted efforts to bolster revenue and curb costs. The resulting savings led to actual expenditures for the year that were approximately 1% below budget authorizations, i.e., the actual expenses of \$24,136,307 were below budget by \$261,296. As a result of the measures to ease pressures on the budget, APA realized a surplus from operations in 1991 of \$126,774, which amounts to roughly 0.5% of the budget.

The practical benefit of this modest surplus is that it will help reduce

TABLE 1. APA Balance Sheets as of Dec. 31, 1991 and 1990

Item	Amount (dollars)	
	1991	1990
Assets		
Current assets		
Cash and cash equivalents	2,365,187	1,451,734
Marketable securities	—	652,561
Accounts receivable, less allowance for doubtful accounts	1,491,874	1,387,536
Grants and contracts, approved and in process	2,207,835	2,172,286
Advances to affiliates	1,607,283	1,128,239
Publications inventory	493,486	495,093
Prepaid expenses and other current assets	397,635	396,004
Total current assets	8,563,300	7,683,453
Property and equipment		
Land	5,187,470	5,187,470
Building—leasehold interest and improvements	7,073,142	7,104,926
Furniture and equipment	2,595,327	2,446,675
Subtotal	14,855,939	14,739,071
Less accumulated depreciation and amortization	3,321,215	2,804,993
Total property and equipment	11,534,724	11,934,078
Other assets		
Deferred expenses, net of accumulated amortization	3,294,313	2,615,926
Deferred land rent	770,337	809,578
Intangible pension asset	—	231,307
Total other assets	4,064,650	3,656,811
Total assets	24,162,674	23,274,342
Liabilities and fund balances		
Current liabilities		
Accounts payable	617,141	1,381,929
Accrued expenses	2,257,222	1,865,145
Deferred revenue	1,765,281	1,344,300
Deferred amounts		
Restricted—grants and contracts	2,017,054	1,508,808
Restricted—awards and special projects	2,616,820	2,165,160
Total current liabilities	9,273,518	8,265,342
Other liabilities		
Capital lease obligation, less current maturities	4,414,996	4,430,070
Accrued pension cost	—	231,307
Total other liabilities	4,414,996	4,661,377
Fund balances		
Unappropriated	6,204,816	6,078,042
Appropriated	150,000	150,000
Building	4,119,344	4,119,581
Total fund balances	10,474,160	10,347,623
Total liabilities and fund balances	24,162,674	23,274,342

Americans contended with losses in their confidence in the economy, their financial security, and their jobs. The economy stalled again last year, in part because of a continuation of recessionary pressures. The economy was further weakened by a restructuring of many corporations (General Motors was a prime example) that were striving to trim costs and enhance efficiency. As a practical matter, the entire process was termed "the recession" by the media and most of the citizenry, and the results were as negative as the label.

At this point I should briefly mention something that has been discussed in detail in earlier Treasurer's reports, namely, that APA currently operates on a business cycle, just as many organizations do. This means that the Association has some financially strong years, then some weak years, then the cycle continues. Although a mechanism has been put in place to smooth out the business cycle in the future, it was in full effect in 1991. The point is that the recession hit

TABLE 2. APA's Functional Revenues and Costs for Fiscal Years 1991 and 1990

Item	1991	1990
Functional revenues		
Percent from each function		
Publications		
Advertising	16.50	18.84
Subscriptions and related fees	8.22	6.72
Book sales	15.78	16.65
Member services		
Dues from members	39.02	36.40
Meetings income	13.22	12.78
Other income related to member services	2.38	2.37
Other income (investments, overhead on grants, contributions, etc.)	4.88	6.24
Total revenues (dollars)	24,263,081	24,907,182
Functional costs		
Percent for each function		
Governance and member component activities (Board of Trustees, Assembly, joint commissions, councils, and components)	16.26	15.50
Publications (APA journals and book sales)	29.77	29.76
Public affairs (public information and government relations)	10.15	10.33
Member services (membership services and educational programs)	26.12	27.16
General administrative costs	17.70	17.25
Total costs (dollars)	24,136,307	24,257,444

at exactly the same time as APA hit a low point in its own business cycle.

Although the federal government reports that the recession started in August 1990, economic data show that the economy was actually in decline in the spring of 1990. Although some APA revenue-producing programs experienced a revenue downturn early in 1991, these shortfalls were offset by strong revenue production by other programs for the first 9 months of the year. As a result, APA's overall financial operations did not show the symptoms of recession until October 1991. In other words, the recessionary pressures that were causing serious problems for many companies in the spring of 1990 did not have a heavy impact on APA until 1½ years later. While this was good fortune for the Association, our good fortune was enhanced by our own efforts to stimulate revenue, cut costs, and maintain strong ties with a weakened banking community.

APA revenue fell short of estimates for 1991 since recessionary pressures on the Association were pronounced during the last 4 months of the year. Nevertheless, revenues were maintained close to budget estimates because of very positive book sales, annual meeting receipts, and subscription sales for the *American Journal of Psychiatry*. In addition, financial support from grants and contracts from the federal government and private foundations enabled the Association to provide a number of needed products and services without placing an additional burden on our fiscal resources.

Although the impact of the recession on APA was not significant until late in 1991, this problem had been predicted many months in advance. The projected revenue shortfall was communicated to component chairpersons and department heads early in the year, and they were urged to stimulate revenues and carefully monitor expenditures. It was only through the diligence of our member and staff leaders in working to bolster revenue and to keep costs in line with budget estimates that a break-even budget was achieved. Certainly, the financial crunch was felt throughout the organization as a freeze was placed on filling new positions, equipment purchases, and travel. But the result was worth it. Expenses were not only enough below budget to

offset the revenue shortfall but were enough to generate a surplus from 1991 operations as well.

DEBT MANAGEMENT

As a result of effective cash management, borrowing on the Association's seasonal line of credit in 1991 was held to \$2 million. At year end, all drawings on the line of credit had been repaid in full. Projections indicate that borrowing will increase during the remainder of 1992 and throughout 1993, reaching a high point of \$6.5 million in 1993.

APA has continued to maintain a solid relationship with local banks despite a continuing deterioration of the financial position of banks in general and a growing reluctance of banks to provide favorable terms or even to make loans. In fact, one of the primary reasons cited for the heightened level of corporate bankruptcies in recent years has been the inability of many corporations to obtain renewals of bank loans.

During this period of a weakening banking community, APA has not only obtained bank loans as needed but has obtained loans with favorable terms. Highlights of the Association's current loan package are as follows.

Term loan—maximum limit of \$1,500,000 at ½% over the prime rate. As of Dec. 31, 1991, there were no borrowings through this mechanism. Any future borrowings are due and payable by Oct. 1, 1993.

Line of credit—maximum limit of \$5,000,000 at ½% over the prime rate. The stability of the cash budget was evidenced by the fact that the line of credit was used during only 4 months of 1991 and only \$2,750,000 of the line needed to be used.

The hallmarks of APA's debt management in the past have been to maintain ongoing liaison with selected local banks, to maintain a sound financial position, and to honor all commitments to banks, including the repayment of all loans fully and on time—with no exceptions. Although this debt management posture has stood APA in good stead, the Association is moving to a higher level of debt management. We are assuming a more aggressive and proactive stance with respect to borrowing by reducing the amount of borrowing in the first place. APA is moving to a position of self-sufficiency.

NET WORTH

The Association's stated net worth (reserves) has increased from approximately \$4 million in the mid-1970s to roughly \$10.5 million today (\$10,474,160). This stated figure is extremely conservative, since it does not include the estimated appreciation in value of the 1400 K Street property purchased by APA in 1980. The increase in net worth is particularly impressive in recent years, even after the impact of inflation is considered, from \$7,486,501 in 1984 to \$10,474,160 as of Dec. 31, 1991. As noted elsewhere in this report, the Association is planning not only for continued growth of its net worth but for an enhancement of liquid (cash) net worth.

STRATEGIC FINANCIAL PLANNING

The Budget Committee, through its Financial Planning Subcommittee, has moved ahead in its efforts to set a strategic fiscal agenda for the Association. The subcommittee has met twice since its establishment by the Board of Trustees in March 1991. Working on a 3–5-year planning time frame, the subcommittee had established a series of APA fiscal goals by August 1991 and, in addition, had assigned staff specific tasks relative to the implementation of those goals. Following are highlights of progress in the establishment and achievement of these fiscal goals.

Reduction of Borrowing Through Development of Liquid Reserves

APA's target for liquid reserves is an amount equal to 3 months of staff salaries, i.e., \$1.8 million. As mentioned earlier, the Association's surplus from 1991 operations of \$126,774 is an initial step

toward this goal. The 1992 budget contains provisions for a cash operating surplus of \$300,000 to add to liquid reserves. The strategic financial plan calls for an aggregate cash operating surplus amounting to \$1.5 million for the 4-year period 1993 through 1996 to achieve this target.

Smoothing Out of Business Cycle

The peaks in the APA business cycle are the result of strong revenue, and the troughs in the cycle stem from weak revenue. Plans are currently in place to begin smoothing out the Association's business cycle at the time of its next peak, which is expected in 1994. This will be accomplished by shifting revenue from stronger to weaker years.

Review of Total Employee Compensation, Including Salaries and Fringe Benefits

Future reviews and deliberations regarding staff salaries and fringe benefits are to be conducted within the context of total compensation. APA's staff and consultants began working on this assignment during the last quarter of 1991. Using a nationwide survey by another medical specialty, APA has compared the salaries and benefits of its higher-salaried staff with those of other medical specialty associations. It was found that the salaries and fringe benefits provided by APA are well within the ranges of those of other medical specialty associations having annual budgets of \$20 million and more. APA is participating in several local salary surveys and will use the results of these surveys in the review of total compensation of lower-salaried staff. However, these efforts are only a beginning. As the Association attacks the problems of ongoing salary reviews, the costs of staff benefits, and many other related matters, these complex issues will be considered within the context of total employee compensation, using our rapidly growing data base in this area.

Exploration of Options for Managing Investments and Improving Their Performance

In the mid-1970s approximately 60% of the Association's asset base was contained within its investment portfolio. For this reason, APA established the Investment Advisory Committee, comprising well-known and successful financiers from the Washington, D.C., area.

The investment portfolio has now been reduced in size to only 3% of the Association's asset base because the majority of APA's investments relate to the 1400 K Street building program. Oversight of the portfolio now rests with the Asset Management Advisory Committee, composed of two members of the APA fiscal staff and two consultants in the areas of finance and benefits, respectively. The assets of the portfolio are currently folded into the larger portfolio of the Washington, D.C., financial institution ASB Capital Management to achieve the benefits of greater diversification of investments.

Streamlining of Operations Through Reorganization and Automation

The Association has achieved budget savings and operating efficiencies through departmental reorganization, computerization of numerous activities (including budgeting and financial forecasting), and other technical enhancements, such as desktop publishing. Similar proposals are currently being developed, and component chairpersons and department heads will be encouraged to contribute ideas as they develop their 1993 budget proposals.

Implementation of Capital Budget

The 1993 budget package will include not only the traditional annual operating budget but also a capital budget. The capital budget will focus on requests for new facilities, such as additional or improved office space; equipment purchases (computer or communications hardware, for example); multiyear research or program development projects, such as DSM-IV or the *Biographical Directory*; grants from governments or foundations, provided full overhead is

allowed by the grantor; and gifts from corporations or individuals to support specified APA programs, provided matching is not required from the APA general fund.

Identification of Means of Strengthening Balance Sheet and Profit-and-Loss Statement Without Increasing Member Dues

The Financial Planning Subcommittee has identified a number of potential programs for producing nondues revenue. The feasibility of implementing the potential programs is being explored, and this exploration includes market research and discussions with other associations and consultants. Efforts to curb costs have been discussed throughout this report. Some of the most effective cost-control efforts

include freezing various expense categories and systematically monitoring budget implementation.

Development and Prioritization of Mission and Goals

It is envisioned that the Budget Committee will serve as a catalyst for APA leadership to develop a crisp statement of APA's missions and goals. The next step is one that has proven to be difficult in the past, i.e., the prioritization of the mission and goals. As challenges to the field of psychiatry mount, and as the financial resources to meet those challenges fade, prioritization becomes essential. Although this goal is stated last on this list, it could well prove to be the key to all other goals and, thus, the most important goal of all.

Report of the Medical Director

Melvin Sabshin, M.D.

During my tenure as APA Medical Director, this report has become a useful reflection of progress and problems. We have indeed been coping with remarkable challenges; the themes of socioeconomic and political ferment have dominated my reports for some time. The coping process has been accompanied by an increased diversity and complexity of the functions assumed by the national leadership and the Central Office. Since last year's report, we have faced many difficult decisions and actions. There has been a leveling off in our membership, accompanied by a drop in the number of medical students choosing residencies in psychiatry. Psychiatry has been in the limelight in the media primarily in relation to ethical breaches, and there has been an increase in reporting and awareness of sexual interactions with patients. The "Frontline" television program attacked not only the profession but also the Association for its alleged role in a complex malpractice situation related to ethical issues. At the same time, we have had numerous successes, and I am pleased with the mood, strength, stability, productivity, and responsiveness of the organization. Both the tone and content of our activities are positive overall and demonstrate strong, effective working relationships between staff and members. Dr. Hartmann's thoughtful, dynamic, and effective leadership is reflected in the strength and enhancement of many departments' efforts.

APA staff has shown remarkable efficiency and productivity. While the quantity of work continues to increase, we have been able to maintain high quality, even in the face of increasing demands in many arenas. This year the Association has focused on how to provide the most cost-effective support and leadership for the diverse needs of more than 37,000 members while avoiding possible fragmentation resulting from increased interest in subspecialization and a variety of forms of practice. We have devoted much energy to consideration of the impact of managed care on APA members and their patients. Through extensive resources devoted to scientific activities, we are developing practice guidelines, as well as continuing to develop a reliable and valid diagnostic nomenclature. Our strength in public policy deliberations and in the decrease of stigma associated with care for mental disorders has depended heavily on our scientific growth and credibility as a field. We also have carefully monitored the Association's business-related work and fiscal affairs, as well as the more traditional specialty society membership efforts. To that end, we have queried our members through focus groups, paid careful attention to their written and oral comments, and have held frequent discussions with our counterparts in other medical specialties and mental health disciplines.

Currently, there are three search processes for senior positions in

various stages of completion. The search advisory committee charged to assist us in identifying a Director of the Office of Education, with members Drs. Jerald Kay, Paula Panzer, James Shore, and Joel Yager, has completed initial interviews of nearly a dozen psychiatrists. We are pleased at the interest shown by these candidates, who have broad experience in psychiatric education and administration. Some members continue to express concern that we have accepted outside funds for the position. We understand the considerations expressed and wish to avoid even the appearance of any control by an outside organization or industry. The funding has been given to APA without any encumbrances; Abbott Laboratories has had no involvement in any aspect of the search process, nor will it influence any aspect of the operation of the Office of Education. We do not see this important position as solely funded by an outside firm; rather, this donation enables us, particularly in these tight fiscal times, to recruit a psychiatrist director who will bring considerable experience and involvement to the position. We had delayed filling the position because of fiscal constraints. Ms. Rosalind Keitt, Interim Director, has been an extraordinarily effective leader who has worked well with the Council on Medical Education and Career Development and related educational organizations. She and Office of Education staff, as well as Drs. Spurlock and Robinowitz, are to be commended for their prodigious efforts in strengthening our educational productivity and performance. At the same time, members of the educational community have voiced their concerns that we fill the position as soon as possible, noting the importance of the position to psychiatry. (Since this report was written Dr. Jay Scully was named Director of the Office of Education.)

Dr. Jeanne Spurlock retired on Dec. 31, 1991, after nearly two decades of extremely devoted and effective service to APA. Dr. Spurlock has been an extremely articulate advocate for underrepresented groups—and her efforts did much to promote the quality of care delivered to minority populations, expand opportunities for minorities within the Association, and increase our awareness and understanding of issues affecting minority populations. The search for her successor also is under way. Ms. Hart, working with Dr. Robinowitz, will provide staff support to the search committee, which is chaired by Dr. Robert Phillips and has as members Drs. Donna Norris, Pedro Ruiz, and Dale Walker. A position description has been circulated, and we have already received excellent suggestions from the field.

I appreciate the remarkable efforts of Ms. Linda Roll, who, as Interim Director of the Office of Minority/National Affairs, is providing excellent staff assistance to our councils and components and supporting many activities in this area. I also appreciate the substantive

consultation provided by Drs. Spurlock and Henry Work to the Office of Minority/National Affairs in this interim period.

In November 1991 Dr. John Nemiah announced his intention to retire from his position as Editor of the *American Journal of Psychiatry*. Under his superb stewardship, the *Journal* has grown in scientific stature, while maintaining its literary excellence and readability. Dr. Nemiah has brought in the best of modern technology, while enriching the scholarly nature of our publication. He has led with wit, warmth, and grace. His working relationship with Deputy Editor Dr. Nancy Andreasen, Managing Editor Ms. Sandra Patterson, and staff has been exemplary. Dr. Hartmann has appointed a search committee charged to recommend his successor; this committee is chaired by Dr. Herbert Pardes, with members Drs. Glen Gabbard, Judith Rapoport, George Vaillant, and Joel Yager. Receiving staff support from Dr. Robinowitz, they too have requested suggestions of possible candidates from the field and have met with Dr. Nemiah and staff to develop criteria for the position. From the initial list of some two dozen candidates, they have identified 10 candidates for further consideration.

In September 1991 Dr. Marta De Titta, Director of the Office of Membership, resigned to return to her native Argentina. In her tenure at APA, Dr. De Titta brought a combination of energy, understanding, and concern to the work of the Office of Membership, maintaining interest in analysis of membership data and trends, while paying personal attention to each individual member's communication with the Association. I appointed Ms. Elizabeth Thomas, former Assistant Director, to serve as her successor. In addition to her excellent performance as Assistant Director, Ms. Thomas served quite effectively as the "ombudsperson" for our member insurance program. These changes sparked a number of staff position shifts. The Recruitment Coordinator, Ms. Dara Schumaier, was promoted to Special Assistant to the Senior Deputy Medical Director, where she serves half time as the "ombudsperson." Mr. Michael Murphy was promoted to Assistant Director of the Office of Membership, replacing Ms. Thomas.

It is with mixed feelings that I report the promotion of Mr. Murphy, formerly Administrative Assistant to the Assembly. I am pleased and proud of his promotion, which reflects the excellence he brought to his position as Administrative Assistant to the Assembly. Many of you have shared with me your appreciation of his effectiveness, organization, and attention to quality and detail. He brings these excellent skills to the Office of Membership. Additionally, Mr. Murphy has agreed to take on a further task. Ms. Corky Hart has provided staff support for the Joint Reference Committee for more than a decade, bringing her excellence in organization and her knowledge of APA and our components to the task. She has performed admirably and effectively. Over the past 6 months, however, her expanding duties in the Office of Psychiatric Services have infringed on the time available to maintain her high level of involvement with the Joint Reference Committee. Mr. Murphy will take over these efforts in addition to his work in the Office of Membership. He and Ms. Hart will work together to ensure a smooth transition and to work effectively with the next President-Elect and Speaker-Elect. We very much appreciate his willingness, in these tight fiscal times, to take on this added task, and we know that his experience in the Office to Coordinate the Board and Assembly will be advantageous in fulfilling this responsibility.

In October 1991, after 10 years of service to APA, Mr. Charles North retired as director of the Human Resources (formerly Personnel) Department. Mr. North contributed greatly to the development of standards and procedures as we moved from the informality of a small operation to a large professional organization that must address requirements and regulations, as well as problems of both management and support staff. I appointed Ms. Margaret Zieg, Assistant Director, to succeed him, and Ms. Debrah Brown was promoted to Assistant Director. I am most gratified with Ms. Zieg's quiet professionalism as she assists us not only in recruitment, evaluation, education, and retention of staff but also in dealing with benefits and morale enhancement during tight fiscal times.

Among the saddest news this year was the loss of past President Dr. George Tarjan. Dr. Tarjan had been an active contributor to so many activities—serving as a resource for staff and members alike. His constant availability and his cool-headed no-nonsense approach to problems were especially valued. He chaired the *Psychiatric News* Editorial Advisory Board, which reviews both policies and content of

the newspaper. Consultants from other publications (e.g., *AM News*) also provided valuable input. Under the leadership of Dr. Robert Campbell, Editor-in-Chief, and Mr. Herbert Gant, Executive Editor, *Psychiatric News* is demonstrating increased emphasis on meeting members' informational needs. A new section, highlighting psychiatrists' accomplishments and interests, is planned, as is a section containing debates; we also anticipate greater editorial focus.

We also were sad to learn of the death of past President Dr. John Spiegel. He too was a valuable resource to all of us, and his leadership in addressing social problems associated with mental disorders and his efforts to democratize APA's work were pivotal.

No report could be complete without some discussion of the long-term impact of the "Frontline" program. We continue to receive correspondence from members and others concerned with the statements made on the program. We had been unsuccessful in our interaction with the producers to try to correct the inaccuracies and misrepresentations in the program, nor did we persuade them to provide information to viewers about available resources. We appreciate your individual efforts to correct the misinformation. All in all, there have been two dozen phone calls and about 60 letters—mostly from members expressing feelings ranging from outrage at what they (incorrectly) perceived as APA policy regarding undue familiarity, to questions about why APA could not control the defense attorneys for Dr. Richter, to concern that APA had not intervened effectively in advance of the program to prevent its showing. All shared our distress at the impact of the case on Dr. Gay and her patient. I have personally answered each member, as have others in the leadership, and these efforts (in addition to the material included in *Psychiatric News*) made an impact. At the same time, this issue has caused major distress to members who did not choose to contact us. At district branch meetings, interactions with residents, meetings of other groups, and so forth, the topic continues to receive prime attention. The recent publicity over the practices of Dr. Margaret Bean-Bayog also reflects poorly on the field and has a negative impact on access to treatment and how treatment is conducted. While we have much in our ethical activities of which to be very proud, and we have developed strong preventive education programs and implemented responses to violations, much more needs to be done to address public perceptions and misperceptions.

The Division of Public Affairs has revised the "Fact Sheet on Doctor/Patient Sex." The content restates appropriate material from our code of ethics; describes how to file an ethical complaint; provides names and addresses of district branches, other professional organizations, and self-help groups; and includes an extensive bibliography. Copies are available from the division.

APA also issued a press statement on sexual harassment in response to discussions at the Senate hearings to confirm Clarence Thomas as Supreme Court Justice. The statement described the impact of sexual harassment and concluded, "Sexual harassment is destructive behavior that can cause profound psychiatric problems for its victims. It must not be tolerated in any setting."

Other ethical issues continue to be addressed. The misuse and abuse of hospitalization continues to receive publicity that unfortunately affects the entire field, causing even needed hospital admissions to be viewed with suspicion. Not only must we vigorously speak out against such abuse and the systems that engage in it but we also need to develop and publicize clear, scientifically based, reliable criteria for hospitalization.

In response to extensive media reporting of allegations of major problems with psychiatric hospitalization practices in several states and the numerous repeated expressions of concern by key Congressional staff about these allegations, I sent a letter to all members of the U.S. House of Representatives and Senate detailing APA ethical guidelines for hospital admissions. The letter also outlined actions that APA had requested its district branches to undertake. These included dissemination to the local community of information about how to file a complaint of ethical misconduct against a psychiatrist, review of current state psychiatric hospitalization laws, and, where necessary, work with state legislatures to improve those laws.

Similarly, the Dahmer trial had the potential to reinstate controversy about the "insanity defense" and, with it, to attack our diagnostic credibility and reliability. Although similar courtroom controversies exist in other medical specialties, they do not seem to have had

the same negative impact on the public (and other physicians), resulting in a slur on psychiatry—especially our diagnostic and treatment capacities. I was pleased with the quality of coverage and the understanding demonstrated by the media.

Our public affairs efforts must be strong, not only in responding to problems and issues but also in developing proactive strategies for dissemination of positive information and image enhancement. We have had much success in efforts such as Mental Illness Awareness Week, and our film on depression has reached many effectively, but we also must anticipate and, whenever possible, avert problems and use what Dr. Paul Fink has called a “psychiatric SWAT team” to respond to “hot” issues rapidly and effectively.

Dr. Allan Tasman has been a thoughtful and energetic chairperson of the Scientific Program Committee. This year he completes his tenure in that role. Under his direction, the program at the annual meeting has continued to expand in content and sophistication. There has been greater attention to integrating research findings into the scientific educational program and increasing emphasis on more interactive and participatory sessions for clinicians. The annual meeting is a high point of the year, an active and integrating force that mirrors directions for the field.

The planning of the program for this year, under the direction of Dr. Tasman and Dr. Michelle Riba, vice-chairperson, has been stimulating and fulfilling. The broad array of scientific presentations in a variety of formats offers excellent education for all participants. The President's theme has sparked a number of thoughtful and innovative symposia and workshops. The number of courses available has expanded in response to members' requests. Advance registration figures suggest another very well-attended meeting.

Dr. Jeffrey Akman, chairperson of the Local Arrangements Committee, and the committee members have been remarkably effective in identifying a host of leisure-time activities, taking advantage of the museums, institutions, and natural surroundings of Washington, D.C. Dr. English has appointed Dr. John Oldham as chairperson of the Scientific Program Committee for the 1993 meeting, to be held in San Francisco, May 22–27; Dr. Riba continues as vice-chairperson. Dr. English's Presidential theme is “Patient Care for the 21st Century: Asserting Professional Values Within Economic Constraints.” The leadership of the Scientific Program Committee met in March in San Francisco with local leaders and the Local Arrangements Committee, chaired by Dr. Lawrence B. Lurie, to initiate the 1993 planning process.

Because the size of the annual meeting has increased, fewer than a dozen cities have the facilities—both sleeping and meeting rooms—to meet our needs, and these cities are heavily booked. As an example, we cannot obtain space in Chicago or San Francisco until after the year 2000. Thus, we must plan considerably ahead to ensure having the location we want at a time that meets our needs, recognizing that external events may change during this longer lead time. The schedule, as planned, is as follows:

- 1993 San Francisco
- 1994 Philadelphia (Sesquicentennial)
- 1995 Miami
- 1996 New York City
- 1997 San Diego
- 1998 Toronto

The accomplishments of the annual meeting could not have taken place without the devoted efforts of staff. In particular, I would like to recognize Ms. Carol Davis, who has provided oversight and support, as well as her special know-how and experience in so many areas; Mr. George Campbell and staff of the Office of Meetings and Exhibits Management, who have been immensely helpful and whose professionalism has contributed to the positive tone and format of the meeting; Ms. Cathy Nash, Director of the Office to Coordinate the Annual Meeting, and her staff, whose remarkable efforts have provided a smooth, highly organized program; and Dr. Robinowitz, who provides overall supervision. Their creativity, hard work, and resilience enable us to handle this complex, multifunctional large-scale event in a way that provides an opportunity for each attendee to have an enjoyable and useful educational and social experience.

We have reviewed the recently approved guidelines of the Accredi-

tation Council for Continuing Medical Education regarding interactions with industry and have discussed these regulations with the Committee on Exhibitors and Advertisers and with additional representatives of industry. Our planning, review, and evaluation procedures are in compliance with the guidelines of the Accreditation Council for Continuing Medical Education, and we have strengthened the involvement of the Scientific Program Committee with the symposia faculty to ensure broad and representative scientific content throughout.

The Scientific Program Committee, recognizing the concerns about quality and control of industry-sponsored educational activities, continues to review and monitor these efforts closely. Members were pleased with what appeared to be the impact of the discussions held during two meetings with industry representatives this past year. Not only is duplication of topic or presenters absent but the sessions are more broadly based, with less overemphasis on pharmacological issues. A clear effort is being made to address Dr. Hartmann's theme of biopsychosocial integration. Notwithstanding this improvement, the Scientific Program Committee this year did reject several industry-sponsored submissions because they did not meet the rigorous scientific and educational criteria for inclusion in the program. The committee also plans to monitor adherence to the guidelines related to publicizing such sessions and any associated social activities.

An example of the need to oversee relations with industry occurred in November 1991, when we met with representatives of Glaxo Pharmaceuticals regarding its videotape of the forum on managed care presented at the 1991 annual meeting. We were unable to obtain funding for this task, and Glaxo volunteered to make and distribute videotapes of the session. There was considerable delay in proceeding because Glaxo expressed concern about the quality of the product, stating that it was a very one-sided, unbalanced session of simply “bashing” managed care. At the same time, the moderator was quite concerned that the tape was not being produced quickly enough and that it appeared Glaxo was interfering with our judgment about the content of the session. As these concerns were clarified, Glaxo reiterated its willingness to support editing of the tape according to APA specifications and to make clear that the tape and the session from which it was derived were APA's responsibility. We especially appreciate the input and assistance of Dr. English in resolving the conflicts and moving the process along. Dr. Robert Michels, who moderated the original session, and Dr. Ellen Leibenluft from the Scientific Program Committee have completed their review, and the final product is in preparation.

The 1991 Institute on Hospital and Community Psychiatry, held in October in Los Angeles, was a great success by any standard. It exceeded expectations programmatically and fiscally, with more than 250 program offerings and over 1,500 registrants. Under the leadership of Dr. Harold Eist, the Institute on Hospital and Community Psychiatry Program Committee developed an extensive array of enriching offerings on clinical and policy topics. Of special interest were sessions on women, the interface of cardiology and psychiatry, and treatment planning.

The 1992 Institute on Hospital and Community Psychiatry Program Committee, chaired by Dr. David Olenik, met in early January to plan the 1992 institute, to be held in Toronto, Friday, Oct. 23, through Tuesday, Oct. 27. For the first time, the meeting will be held over a weekend to take advantage of reduced air fares. Its theme, “Partnerships for Mental Health: Access, Quality, Cost,” reflects the interests of APA leadership as well as Canadian and consumer representatives.

Full- and half-day sessions will be held on such topics as administrative psychiatry, international mental health programs, the Canadian mental health system, universal access to care, managed care, schizophrenia, substance abuse, AIDS, multiple personality disorder, therapist-patient relationships, and a host of other clinical issues.

We have also begun recruitment of the next group of APA/Mead Johnson Fellows. Eligible are residents who enter the third postgraduate year during the fellowship year. This program strives to heighten residents' awareness of opportunities in the public sector, enhance their training experiences, and familiarize them with programmatic aspects of APA.

We also have been most impressed by the continued growth and excellence of the *Hospital and Community Psychiatry* journal. Dr. John

Talbott's energetic and effective editorial efforts have served the field well. The excellent staff support of Managing Editor Ms. Teddye Clayton and her staff has maintained smooth functioning even during Dr. Talbott's sabbatical.

Last year Dr. Lewis Judd resigned as Director of the National Institute of Mental Health (NIMH) to return to the University of California. During his tenure Dr. Judd displayed great wisdom and effective leadership, increasing both the funding and the prestige of NIMH and the profession. Dr. Judd, in collaboration with the National Mental Health Association, initiated the National Mental Health Leadership Forum, whose members represent major professional organizations and advocacy groups. This forum, in conjunction with the National Advisory Mental Health Council, has held town meetings and hearings, which have been most effective in addressing needs and combating stigma; they have strengthened the planning process for access to and organization of care. The forum's work on public information and image is outstanding. I also would like to express appreciation for the work of Dr. Alan Leshner and his service as NIMH Acting Director during the past year and a half. He has done much to continue the excellence of the institute.

While the saga of the proposed legislative reorganization of the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) and the need to protect the integrity of NIMH research and services continues, it was, and will continue to be, deeply influenced by the resignation of Dr. Frederick Goodwin from his position as Administrator of ADAMHA. Dr. Goodwin resigned as ADAMHA Administrator in response to what we told Dr. Lewis Sullivan, Secretary of the U.S. Department of Health and Human Services, was a "racially insensitive and inappropriate comment about violent behavior," which he made to the National Advisory Mental Health Council at its meeting on Feb. 11, 1992. At the same time, we supported Secretary Sullivan's decision to appoint Dr. Goodwin as NIMH Director because "it would be wrong to punish the mentally ill citizens he has served so well." The National Alliance for the Mentally Ill told Secretary Sullivan that their 150,000 family members commended Secretary Sullivan for Dr. Goodwin's appointment. APA member Dr. Joseph Coyle (President of the Society for Neuroscience and chairperson of the Department of Psychiatry at Harvard Medical School) told Secretary Sullivan that Dr. Goodwin is "an eminent neuroscientist and internationally-recognized psychiatrist who has provided outstanding leadership at ADAMHA." Moreover, while many leaders (including those at the American Psychological Society) supported Secretary Sullivan's decision to name a psychiatrist as Director of NIMH (neither ADAMHA nor any of its other institutes is headed by a psychiatrist), the American Psychological Association actively opposed Dr. Goodwin's appointment.

We all were distressed with the events leading to the resignation and with the impact on the field. Other related serious political and policy consequences, fueled by the controversy surrounding Dr. Goodwin, include the impact of the foregoing on the reorganization of ADAMHA and how to protect the present (tripartite) mission of NIMH because of the essential connection between services and research, scientifically designed demonstration projects, and sophisticated basic biological, behavioral, clinical, and epidemiological research.

Last year the U.S. Senate approved reorganization legislation, placing the research activities of the institutes under the jurisdiction of the National Institutes of Health while maintaining a separate services program under the jurisdiction of the proposed "Alcohol, Drug Abuse, and Mental Health Services Administration." Key members of the House of Representatives initially expressed reservations about the reorganization. At this writing, it appears that the issue was resolved in a House-Senate conference and that the transfer and reorganization are slated for October 1992. We will need to monitor plans and their possible impact closely, and we anticipate working with the academic and consumer communities to ensure the best possible outcome.

The issue of managed care continues to be of great concern to our members. The variations in perception and concerns expressed has been striking. Intrusiveness, the "hassle factor," and awareness of some groups' egregious practices in denying care to those in need are voiced most commonly. At the same time, many APA members work in managed care settings and organizations; some have expressed

strong dissent, noting that APA has not been sufficiently responsive to their concerns and interests, stating that they too are working to promote quality and cost-effective care. Our activities in this arena are broad and varied, and we will continue to support efforts to ensure quality and appropriateness of care. This task has been an interdepartmental staff effort, involving the Office of Psychiatric Services, the Division of Government Relations, the Office of Economic Affairs, and the Division of Public Affairs, working with the Committee on Managed Care, chaired by Dr. Steven S. Sharfstein. We have developed model legislation for standards of managed care, which will be an important resource for individual states. We have met with psychiatrists who hold leadership positions in the managed care industry and have shared members' concerns about practices that interfere with appropriate care.

We have organized meetings with managed care companies to initiate dialogue addressing these problems and provided information to district branches who work with state insurance commissions regarding the need for regulation of utilization review companies. The Division of Government Relations is working to assess the effect of state utilization review legislation, and the Committee on Managed Care is implementing the managed care district branch network.

Staff continues to analyze documented cases reported through the 800 telephone number to assess trends and problem areas. Case information is supplied to district branches for use in negotiations with state insurance commissions regarding the need for regulation of utilization review companies and in monitoring the effectiveness of existing legislation.

Utilization Management: A Handbook for Psychiatrists was mailed to district branches in early spring. Its goal is to educate members in the process of managed care and utilization review. A press conference was held in February to announce the handbook and the *Manual for Psychiatric Quality Assurance* as two of APA's newest efforts in managed care. We continue to collect the medical necessity criteria used by managed care organizations and are developing a criteria library in the Office of Economic Affairs to facilitate review and evaluation of such criteria by the Committee on Managed Care in conjunction with the Committee on Quality Assurance.

The Utilization Review Accreditation Commission, on which APA has board representation, issued its first *National Utilization Review Standards*. These include procedures for review determination, appeals, and confidentiality; staff and program qualifications; and the process for accreditation by the Utilization Review Accreditation Commission.

We also are continuing to document problems with state Medicare carrier operations and are interacting with the U.S. Health Care Financing Administration regarding overall policy, as well as with individual district branches for negotiations with local carriers.

Work is under way to update the *Coverage Catalog*, which will include information about managed care features in employee health plans, and to update the information in the *Marketing Manual*, with a new section on marketing medical psychotherapy. An article on clinical marketing is under development.

In each annual report, I have given special emphasis to our activities in government relations and public affairs. This year is no exception; indeed, I still rate these as the highest-priority areas for producing genuine advances in diminishing stigma while increasing access to and reimbursement for care. Working in concert with our Joint Commission on Government Relations, Dr. John J. McGrath, chairperson, and with commission members and network leaders, the Division of Government Relations continues to function as a sophisticated, effective force.

From my perspective, during this past year we have been much more visible and successful in our government relations activities than ever before. We have begun to develop clear and concrete objectives that have had an enormous impact on members and the patients they treat. We are most fortunate to have Mr. Jay Cutler leading our government relations efforts. He is widely respected on Capitol Hill and in the Administration, as well as by his colleagues. Our successes are a credit to his energy and knowledge and to the long-range strategic planning and involvement of the field in Congressional communications.

The President's State of the Union message contained a strong and politically partisan tone, reflected in the work of the second session

of the 102nd Congress, which already is demonstrating election-year stresses through an unusually partisan climate of debate.

The prospects for health care reform are complex. The Senate Finance Committee approved very limited reforms, targeted at small-market health insurance; the Senate Labor and Human Resources Committee, which already approved the Mitchell-Kennedy "pay-or-play" plan, is expected to consider small-market reform legislation. Similar action is expected by the House Energy and Commerce Committee and the House Ways and Means Committee. These deliberations mask deep-seated disagreements about the scope and direction of health care reform, most particularly as to whether to take limited action aimed at the small market or to risk confrontation with each other and the White House over broader national reforms.

At the same time, it is essential to appreciate political reality; health care reform has so far proved easier for federal legislators to debate than to enact, since support has yet to coalesce around a single legislative proposal. The President's plan includes incentives to encourage Medicare and Medicaid beneficiaries to enroll in managed care plans; limited tax incentives for the purchase of health insurance; medical liability reforms; insurance industry reforms, including preemption of state benefit mandates and state regulation of anticonsumer managed care and utilization review practices; and a sweeping restructuring of the Medicaid program. APA cannot endorse this plan, as it would undercut the strides made in mandating mental health benefits and curbing abusive managed care practices. The Mitchell-Kennedy "pay-or-play" plan, while approved by the Senate Labor and Human Resources Committee, has little support outside of Congress. It is opposed by the insurance industry, and President Bush is reportedly prepared to veto it should it be approved. Intense activity can be expected as both political parties jockey for position as they head into the 1992 national elections.

APA has managed to ensure that most of the key proposals for health care reform include at least some coverage of psychiatric services. The coverage is limited in scope and duration because of Congressional perceptions (fueled by small businesses and the insurance industry) that coverage of psychotherapy and counseling provided by the broad range of mental health professionals included under each state's scope of practice and licensure laws is not necessarily a basic necessity or medically necessary service.

In a related development, APA is working with Representative Mike Kopetski (D-Ore.), a founder of the Congressional Mental Illness Task Force, to develop a Sense of Congress resolution, noting the needs of the mentally ill and stipulating that any comprehensive health care reform legislation include comparable coverage for mental health care. APA also has urged the repeal of the discriminatory 50% copayment requirement for outpatient mental health care under the Medicare program.

The new Medicare fee schedule, based on the resource-based relative value scale (RBRVS), went into effect on Jan. 1, 1992. APA launched a massive and successful effort to correct major errors affecting psychiatry, as published in the June 1991 RBRVS Medicare fee schedule proposed by the Health Care Financing Administration (HCFA). APA work on the RBRVS is ongoing, under the leadership of Dr. Donald Scherl; despite the improvements in the final Medicare fee schedule for psychiatry relative to the 1991 report, many problems remain. APA's most recent comments were filed in late March. Despite this general success, APA members may be adversely affected by several other factors, most notably the geographic adjustment for payments to physicians practicing in relatively high-cost urban areas. We have undertaken a massive educational effort for our members, which will continue as the process evolves. Additionally, the RBRVS work group, consultants, and individual APA members continue to identify and highlight remaining problems adversely affecting psychiatry.

The final version of the fiscal 1992 ADAMHA appropriations bill has been signed into law. NIMH research funding received a 10.9% increase over fiscal 1991. All NIMH programs in the aggregate received a 9.5% increase over fiscal 1991, a significant victory for APA advocacy. The Bush Administration's proposed fiscal year 1993 budget would provide for a \$184 million increase in total ADAMHA funding over fiscal year 1992, with a \$62 million increase in research funding, a \$21 million increase in funding for substance abuse prevention, and a \$4 million increase in demonstration project funding.

We are working with other mental health organizations to develop recommendations for ADAMHA appropriations for fiscal year 1993.

We have submitted comments to the Office for the Civilian Health and Medical Program of the Uniformed Services (OCHAMPUS), addressing proposed reauthorization requirements for mental health services under CHAMPUS, new statutorily reduced inpatient and residential treatment center limits, and a proposed new psychiatric partial hospitalization program benefit. We opposed implementation of the preauthorization program before the October 1991 statutory mandate. We argued that CHAMPUS must better recognize and emphasize the role of psychiatrists in the delivery, authorization, and review of CHAMPUS benefits. APA's comments particularly focused on the critical role of the psychiatrist in the inpatient setting. We strongly supported the new CHAMPUS psychiatric partial hospitalization benefit. Citing APA experience in working with the HCFA on the Medicare partial hospitalization program, we offered to work with OCHAMPUS to better define the parameters of the program.

We urged withdrawal of proposed regulations that would remove existing CHAMPUS medical supervision and referral requirements for marriage and family therapists, mental health counselors, and pastoral counselors. If implemented, this proposed regulation would vitiate any requirements for medical necessity of care and treatment and, further, ignore the need for medical differential diagnosis of CHAMPUS patients or even any evaluation by mental health professionals at the level of a licensed clinical psychologist or clinical social worker. Finally, we noted that it was inappropriate for OCHAMPUS to usurp the traditional state role in regulating the professions by promulgating new federal criteria.

No action was taken in 1991 on legislation introduced by Representative Gary Ackerman (D-N.Y.) to reform the Federal Employees Health Benefits Program, although Representative Ackerman has stated that the House Post Office and Civil Service Committee will hold hearings on the proposal later this year.

APA efforts to ensure that Medicare supplemental insurance ("Medigap") plans cover the current 50% beneficiary copayment for Medicare outpatient mental health treatment have produced a major victory. The Omnibus Budget Reconciliation Act 1990 budget bill required the National Association of Insurance Commissioners to revise uniform minimum standards for Medigap insurance policies. The model standard would, among other provisions, require all Medigap policies to cover the Medicare 50% copayment for outpatient mental health care. I wrote to the National Association of Insurance Commissioners, commending them for their action to end discrimination against the mentally ill and urging them to widely publicize the coverage requirement. In January I also wrote to HCFA Administrator Ms. Gail Wilensky to urge that the HCFA make certain that the mandatory coverage requirement is explicitly stated in forthcoming regulations. On Feb. 21 APA received a response from Mr. Robert G. Eaton, Acting Administrator for Program Development, noting that the HCFA and the National Association of Insurance Commissioners agree that "a Medigap policy must pay the coinsurance for Part B services, which in the case of certain outpatient psychiatric services is effectively 50%." This letter attests to the success of our efforts to end this aspect of discrimination against mental illness treatment.

Intensive efforts helped defeat a last-minute surprise effort to amend the Medicare part A hospital conditions of participation to permit clinical psychologists to supervise care of hospital inpatients. The amendment, authored by Representative Pete Stark (D-Calif.) was felt to be needed because the HCFA allegedly had threatened several hospitals in California with decertification for violating Medicare rules by giving psychologists the right to admit and discharge patients without any physician involvement; the hospitals were responding to the *CAPP v. Rank* decision. At least one of the two hospitals has since changed its rules to avoid conflict with Medicare regulations. Our staff-to-staff contacts brought us an otherwise unavailable document and enabled the Association to voice strong objections to the clinical psychologist provision contained in this amendment. APA argued that it was not technical in nature, that it would have a profound impact on hospital admitting and staffing practices throughout the nation, and that it was yet another attempt to achieve by federal fiat the "medicalization" of psychology. In particular, we argued that it would improperly affect debate in the California legislature to clarify the intent and scope of the *CAPP v. Rank*

ruling. With the vigorous support of the California and Texas district branches, we helped persuade the Senate to defer action on the technical corrections legislation. We expect that Senator Jay Rockefeller (D-W.Va.) will offer the amendment when the Senate Finance Committee considers the bill. Prospects for defeating the amendment are not good, given past Finance Committee support for clinical psychologist legislation.

Four clinical psychologists are in their first year of training at the Uniformed Services University of the Health Sciences under the U.S. Department of Defense psychologist prescribing demonstration program. They are studying gross anatomy, biochemistry, and physiology as part of their first-year didactic program. As part of their patient care training, each psychologist will be expected to "manage," under supervision, 100 psychiatric patients at Walter Reed Army Medical Center. At no time will they be permitted to prescribe independently. Informal reports suggest that some of these trainees are having difficulty with the content of the program and are being permitted to audit the medical courses and are excused from the oral and written examinations required of the medical students.

The fiscal 1992 Department of Defense appropriations bill passed by the House of Representatives included committee language that stated that the program "is only a demonstration, and the Department [of Defense] should not plan any follow-on program or utilization of these individuals to prescribe drugs without written approval of the Congress." In contrast, the Senate version of the defense appropriations bill noted that the "committee feels strongly that this program should be allowed to continue with prohibitions." The final conference report on the compromise bill noted only that the "conferees support the bill language contained herein providing for a two-year prototype drug prescribing training program of military psychologists at Walter Reed Army Medical Center."

The House of Representatives has repeatedly sought to limit the Department of Defense demonstration program but has been unsuccessful, chiefly because Senator Daniel Inouye (D-Hawaii), the program's chief proponent, is the chairperson of the Senate Defense Appropriations Subcommittee and thus is in the key position to ensure survival of this program.

The Senate version of the fiscal 1992 defense appropriations bill included a requirement that the Assistant Secretary for Health Affairs report on "the extent to which military psychologists are currently provided hospital privileges (admitting, discharge, and treatment privileges)" and stated that the "Committee feels that a uniform policy (on admitting) would be more appropriate and further urges the Secretary to institute a permissive policy." The House version of the bill responded to APA advocacy and included no such report requirement or statement of concern about admitting privileges. The Senate language was dropped in the final conference report.

Legislation permitting psychologists to have hospital privileges was introduced in nine states: Louisiana, Massachusetts, Michigan, New Jersey, New York, Ohio (enacted), Pennsylvania, Texas, and Wisconsin. The California legislature continues to struggle with efforts to clarify the *CAPP v. Rank* ruling.

Although no final action was taken in 1991, the Senate Labor and Human Resources Committee and the House Education and Labor Committee each approved legislation (S. 1150 and H.R. 3553) to reauthorize the programs of the Higher Education Act. In a move that stunned the entire medical community, both committees sought to end the current 2-year deferment of repayment of student loans by medical residents, effective Oct. 1, 1993. This unpublicized action allegedly stemmed from committee efforts to obtain paper savings to offset spending elsewhere in the budget.

APA joined with other medical specialty societies, under the auspices of the American Medical Association (AMA), in sending a letter to Congress urging that the termination of the 2-year deferment be rejected. We also sent an "Action Alert" to directors of residency training programs, chairpersons of departments of psychiatry, psychiatry residents, and Medical Student Members, informing them of the proposed change in policy and urging that they inform federal elected officials of their opposition. Numerous letters have been sent to date. The Senate considered the bill in late February and agreed to permit continuation of the 2-year deferment but only for student loans taken before July 1, 1993. House action is expected this month.

We are very pleased that both the House and Senate have approved

legislation incorporating parts of APA recommendations regarding international medical graduates (IMGs). Both bills would establish an Advisory Council on Medical Licensing to monitor the AMA's proposed private system of credentialing IMGs. The advisory council is to report by 1996 on whether the private system is operating effectively. If the AMA's system is not operating effectively, a national system may be established in its place.

We also are pleased at the AMA's efforts with state licensing boards, state and county medical associations, and specialty societies to assist them in developing a strong infrastructure for IMGs and to integrate our concerns into their overall agenda and lobbying efforts.

In December we learned that the AMA had awarded a small grant to APA to support mini-forums on the principles of the AMA Health Access America plan, in conjunction with Area council meetings. The program, which in no way implied endorsement of the Health Access America plan, was designed to foster dissemination of information about the AMA plan for universal access to APA leaders and support dialogues between members and Area business leaders. These sessions provided an opportunity for greater education on issues faced by business and industry in providing health benefits and offered an opportunity to interact with business and industry leaders to inform them about the need for mental health care and problems with access to such care.

APA's representation in the AMA House of Delegates has been forceful and effective. Delegate Dr. John McGrath and Alternate Dr. Ronald Shellow have worked with the Section Council on Psychiatry and with other members of the House of Delegates to support ideas and resolutions. Dr. Richard Steinhilber, through his membership on the AMA Council on Scientific Affairs, has been able to influence areas of AMA scientific investigation. We were pleased that Dr. Douglas Skelton was elected to that council. The representation of the American Academy of Child and Adolescent Psychiatry in the House of Delegates and representation of APA and the American Academy of Child and Adolescent Psychiatry in the Resident Physicians' Section and Young Physicians' Section have been most productive.

While all of APA's suggestions regarding the *Physicians' Current Procedural Terminology (CPT)* are still to be accepted, our input (with the substantial support of Dr. Tracy Gordy, who was appointed to the AMA CPT Editorial Panel, and assistance from Dr. Chester Schmidt) resulted in acceptance of three new interactive therapy codes for the 1992 CPT. We have developed sample vignettes dealing with levels of service for use with the evaluation and management codes, now being reviewed by the CPT Editorial Panel. (An educational packet including information on the new evaluation and management codes, the new interactive psychiatric medical codes, and the psychiatric examples of the new outpatient and inpatient visit codes has been developed for distribution to members.)

I was delighted to be appointed to a special advisory committee to Dr. James Todd, AMA Executive Vice-President; this participation allows for considerable ongoing communication and supports the continuation of our positive and effective interactions with AMA staff.

In late February we held the first combined Public Affairs and State Legislative Institute, which was highly successful. The more than 300 participants expressed much satisfaction with the format and content and encouraged future joint programs. We received funding from almost two dozen pharmaceutical companies, thanks to the efforts of Mr. Ray Purkis, Director of Advertising Sales. Participation by leaders in state legislatures, the insurance industry, the media, and other medical specialties was excellent. The sessions covered such topics as managed care, access to care, prescribing by psychologists, psychiatry's image, and work with the media. The institute offered hands-on skill-building experiences. We congratulate Mr. Jay Cutler, Mr. John Blamphin, and staff in the Divisions of Government Relations and Public Affairs for providing this excellent learning opportunity and meeting the demands of coordinating these sessions.

APA is again working with Senator Paul Simon (D-Ill.) and Representative Ron Wyden (D-Ore.) to introduce this year's Mental Illness Awareness Week resolution. This excellent example of the best in staff interdepartmental functioning and national-local collaboration has become both year-long and international in scope. I would like to commend especially Mr. Cutler and Ms. Phyllis Greenberger for their continued success in this important arena. For the 1991 Mental Illness

Awareness Week, the Division of Public Affairs developed an array of public information materials for journalists and clergy, as well as providers and consumers. District branches conducted public information campaigns in almost every state. The "hometown" radio broadcasts reached a huge audience. Dr. Harvey Ruben conducted a special national 3-hour "Talknet" program with special guests that included Ms. Rosalynn Carter, Dr. Elissa Benedek, and Dr. Lawrence Hartmann.

We have been quite involved in public affairs functions. In his capacity as chairperson of the Joint Commission on Public Affairs, Dr. Harvey Ruben has provided energetic and wise leadership over the years, working closely with Mr. John Blamphin, who heads our staff division. Dr. Ruben's tenure as chairperson concluded this May. He is being honored by the National Mental Health Association for his effective vision and leadership in public education. We also look forward to our work with the incoming chairperson, Dr. Edward Hanin. Collaborative projects with industry have helped enhance psychiatry's image with other physicians and the public. The joint effort with the Upjohn Company has supported several activities. The third film produced in this venture, "Depression: The Storm Within," premiered last year at the American Film Institute Theater at the Kennedy Center in Washington, D.C. Recipient of a prestigious CINE Golden Eagle award from the Council on International Nontheatrical Events, it has been extremely well received by viewers—psychiatrists, other health and mental health professionals, and laypersons. The other two films and related campaign materials have been designed to convey such messages as mental illnesses are real illnesses that cause pain and disability to millions of Americans; they can strike anyone; and they can be diagnosed accurately and treated effectively. The messages also clarify who psychiatrists are and what they do, as well as emphasize the impact of scientific advances. All three films have been seen by nearly 1.5 million people nationwide.

We also have reached over 10,000 physicians and other health professionals through workshops on panic disorders. The materials include an educators' guide to mental illness awareness that suggests curricula, provides camera-ready materials, and identifies local APA contacts. The comic book "Let's Talk About It," designed for junior high and high school audiences, has been well received by more than 64,000 teachers and students. Similarly, we have distributed almost a million products (e.g., pamphlets, posters, bookmarks) related to the "Let's Talk About Mental Illnesses" campaign. The Division of Public Affairs has responded to requests for information about mental illnesses and psychiatric treatment and has provided pamphlets on such topics as anxiety, mental illness, depression, and choosing a psychiatrist.

The Public Affairs Network is one of several locally based groups that expands the reach and effectiveness of the Central Office. Other networks relate to government affairs, AIDS, economics/managed care, research, and education (through chairpersons of departments of psychiatry and directors of residency training in psychiatry). They have been important in such efforts as Mental Illness Awareness Week and providing information to Congress and other policymakers. We now have an experienced network of trained leaders who can cope effectively with all varieties of media.

Work on *DSM-IV* has proceeded remarkably well, and Dr. Harold Pincus, Dr. Allen Frances, and staff have been quite productive. Draft criteria for each proposed diagnostic category have been developed and are contained in the *DSM-IV, Work in Progress: Options Book*, which has been distributed widely to members, components, and the Assembly; additional copies may be ordered from the American Psychiatric Press. The book includes a tear-out form for comments, and the field has been invited to send suggestions and comments on any aspect of the options to the APA Office of Research. With funding from the three ADAMHA institutes, we are conducting field trials at multiple sites to assess specific nosologic issues. A grant from the John D. and Catherine T. MacArthur Foundation funds the analysis of data sets that address unresolved issues for *DSM-IV* and the videotape field trial project. Several videotapes will be pilot tested during the video program at this annual meeting. The draft literature reviews on diagnostic issues are being compiled for inclusion in a *DSM-IV* "source book," to be available later this year. Staff has been involved in discussions with the World Health Organization (WHO), NIMH, and the National Center for Health Services to assure compatibility be-

tween *ICD-10* and *DSM-IV*. A conference involving APA and WHO, sponsored by NIMH, is planned for early July.

In keeping with our increased involvement with colleagues in other medical specialties, we have met with representatives of several organizations to discuss the adaptation of *DSM-IV* for primary care physicians. We anticipate that a preliminary draft of the primary care version of *DSM-IV* will be available in 1993.

During the November 1991 Assembly meeting, we received notice of a petition asking APA to vote on a referendum concerning the adoption of *ICD-10*, upon its publication, as the official psychiatric classification system in the United States and delaying the publication of *DSM-IV* at least until 1997. Initially there appeared to be more than the requisite 500 signatures of voting members; however, a review of the actual signatures demonstrated that, because of duplication and listing of some nonmembers and nonvoting members, the petitioners were 43 signatures short. We informed the petitioners and gave them time to produce the additional signatures, but they were unable to do so. Consequently, the item was not on the 1992 ballot, but it may be resubmitted for next year.

As always, I am concerned about the scientific and policy effects, as well as fiscal implications, of such a referendum. While the latter are obvious, in the long run the impact on science and policy may be extremely deleterious. Arbitrary nonscientific, nonclinical decisions do not enhance the field, and such determinations should not be made by popularity or comfort, but rather by evidence.

Congratulations are due Dr. Pincus for his success in obtaining significant funding to support research and field trials related to *DSM-IV* and funds from the van Ameringen Foundation for activities designed to improve recruitment, training, and retention of psychiatrist researchers. He and his staff also are to be commended for their publication of numerous journal articles.

I am pleased at the progress of the NIMH-funded Program for Minority Research Training in Psychiatry, now in its third year, which is administered by the Offices of Research and Minority/National Affairs. In late February eight postresidency fellows were accepted for 1 year of support; five already have completed a year of research training through this program. We also have selected "mini-fellows" to attend the 1992 annual meeting. Once again, the program will include a variety of scientific and mentoring activities.

Dr. Pincus and his staff have received much praise from the field for the quality of *Psychiatric Research Report*. This quarterly newsletter provides considerable information about science policy, funding and educational opportunities, and research programs.

Dr. Pincus, Dr. McIntyre, and Office of Research staff have been very productive in a variety of activities related to practice guidelines. Drafts of the guidelines on eating disorders and major depression have been distributed to over 100 reviewers and consultants. The eating disorders guideline was considered at the May Assembly and June Board of Trustees meetings. (The guideline was approved by the Assembly and the Board.) Work groups for the guidelines on inpatient evaluation and outpatient evaluation have been established; the initial draft of the outpatient guidelines was reviewed at the January meeting of the Steering Committee on Practice Guidelines. Our efforts to obtain NIMH funding for this work have been fruitful; the funds will be particularly useful in supporting staff work and the track II development. Using this grant, Dr. Pincus has recruited a psychiatrist who will take on the staff responsibility for practice guidelines within the Office of Research, working with Dr. McIntyre and the steering committee. We also continue to participate in the AMA Practice Parameter Partnership and Forum. There is substantial interest in practice parameters (standards and guidelines) within organized medicine. The Council of Medical Specialty Societies sponsored conferences on standards development, and the AMA has undertaken a major initiative for specialty societies to address the topic. Drs. John McIntyre and Sara Charles represented APA in these efforts. I am optimistic and enthusiastic about working with other medical specialties on this important project and about the potential impact of such endeavors on the field.

The Office of Survey Design and Analysis has prepared a series of tables describing findings from the Professional Activities Survey. Staff are engaged in a variety of activities focusing on psychiatrists in research and characteristics of psychiatrists who treat alcohol-related disorders.

There continues to be considerable interest in the APA governance process. The increased activities of the Assembly Executive Committee and its evolution as a major force in the governance of the Association were reflected in its interim meeting in September 1991, in the fourth highly successful meeting with the Joint Reference Committee in February 1992, and in its expanding role in assisting the Assembly in planning and implementing actions.

The Joint Reference Committee, too, has strengthened the input of its voting members while maintaining the importance of the participation of council chairpersons and emphasizing its "joint" role, representing both the Assembly and the Board. The Joint Reference Committee increasingly acts not simply as a referring body but also as initiator and developer of proposals and directions. Drs. Hartmann, Pfahler, English, Shellow, and Bridburg are to be congratulated for their thoughtful yet pragmatic approach to both issues and processes. Ms. Corky Hart has been a marvelous resource here, and the outstanding involvement and coordination of Ms. Jeanne Robb and staff in the Office to Coordinate the Board and Assembly make the process work smoothly.

Discussions about the roles of officers and trustees emphasize the increased involvement and interest of Board members, as well as the expanded amount of business on the agenda of each meeting and the need to set aside time for reflection and strategic planning for the Association. This interest is reflected in the ongoing discussion about subspecialization and liaison activities by the Assembly and Board Commission on Subspecialization. The American Board of Psychiatry and Neurology (ABPN) has responded positively to our recommendations to initiate the process for offering certificates of added qualifications in addiction psychiatry and forensic psychiatry. The American Board of Medical Specialties has formally approved added qualifications in addiction psychiatry and is currently reviewing added qualifications in forensic psychiatry. The Commission on Subspecialization, chaired by Dr. James Trench, is considering the request for added qualifications in consultation-liaison psychiatry. We remain cognizant of the potential fragmentation and divisiveness of such efforts and the need to maintain organizational strength while maximizing input from all concerned.

The significant number of members who vote in elections for APA officers and trustees is most gratifying. We remain one of the few large national organizations that conducts a contested election with voting open to the entire membership; our colleagues in other specialties and disciplines continue to voice their amazement that 40% of eligible members vote in the election. The election process is an enormous task for a group as large as ours, and I am impressed by Ms. Carol Lehmann's careful attention to detail and mastery of the multiple issues that must be considered to ensure a fair and accurate election. The process this year was complex, and I especially appreciate the attentiveness of Elections Committee members to compliance with our guidelines.

Last year, immediately after the annual meeting, APA held a joint meeting with the Caribbean Psychiatric Association. Although the participants' response to the meeting was very positive, it was the last such joint meeting. Increasing demands for higher-priority activities coupled with diminished resources make such meetings impractical.

The substantial increase in communication with psychiatrists in Eastern and Central Europe and with the countries of the former Soviet Union led to our very successful bilateral educational project in April. Under the aegis of the Council on International Affairs and funded by a grant from the Upjohn Company, the project funded a group of psychiatrist experts who traveled to Poland, Hungary, and Czechoslovakia, giving lectures, participating in educational exchanges, and donating books and journals to psychiatrists in these countries. We were impressed by the intellectual fervor with which these sessions were greeted and very much appreciate the leadership of Dr. Eugene Feigelson, chairperson of the Council on International Affairs, and the remarkable efforts of staff member Ms. Ellen Mercer to make this complex endeavor so fulfilling. I also am pleased with Ms. Mercer's participation in the Romania Strategy Group, organized by the U.S. Department of Health and Human Services to coordinate the efforts of American organizations working in Romania. Although the needs of children are being attended to by many groups, there has been no evidence that the mental health needs of the population are being addressed comprehensively by American organizations other

than APA. My own visit to Bulgaria was most enlightening, demonstrating the impact of the massive political change on delivery of psychiatric care and the need for our substantive ongoing involvement. Our Office of International Affairs has gained wide respect under the leadership of Ms. Mercer, and this remains a source of special pride and satisfaction. This office provides assistance for psychiatrists in this country and abroad on issues involving education and trans-cultural practice and care.

I was delighted to learn that we will receive a federal contract of approximately \$25,000 for our Hispanic data base project. The advisory committee, chaired by Dr. Fernando Milanes, will be developing a work plan and a survey instrument. Our goal is to prepare a directory of agencies and practitioners engaged in mental health, substance abuse, and social services for Hispanics. The directory will have three parts: Hispanic psychiatrists who are APA members, Hispanic psychiatrists who are not APA members, and agencies. We will use an approach similar to that used in gathering data for the directory of Asian-American psychiatrists. This is an important effort to address the interests and needs of our members and the populations they serve.

Staff in the Office of Minority/National Affairs have been active in many areas, providing voice, support, and recognition of minority issues and issues affecting children and their families. Contributions to the residents' fellowship programs have been especially meaningful to these colleagues and to those of us who interact with them. Dr. Spurlock also has been involved in liaison efforts dealing with medical, mental health, and advocacy groups and has been a most effective spokesperson for the Association.

We continue to maintain active interaction with the leadership of the American Academy of Child and Adolescent Psychiatry. Additionally, Drs. Pincus and Robinowitz continue to be involved in activities related to research and training in child and adolescent psychiatry. Dr. Henry Work assists staff working on child psychiatric activities one-half day a week and oversees our liaisons. We continue to be concerned about recruitment, retention, education, and clinical care, as well as research and research training, in this important area.

I am very pleased that the Kenworthy-Swift Foundation approved our request for a \$25,000 grant to support the work of the Task Force to Study the Use and Abuse of Psychiatric Hospitalization of Minors. Dr. Elizabeth Weller, chairperson of the task force, will consult with staff to define the work plan.

On Jan. 1, 1992, our membership totaled 37,279, for a net gain of 361 during 1991. The number of non-dues-paying members continues to increase faster than the number of dues-paying members. The increase in losses in 1991 resulted in large part from the change in policy that required dropping members who were in arrears for 1990 dues in June 1991 (as opposed to December 1991); there was also a slight decrease in the number of new members. Reinstatements were higher in 1991 (31 more than in 1990). Non-dues-paying members represent 19.5% of the total. Medical Student Members and Members-in-Training total 17.6% of our membership, as compared to 15.6% in 1987. Over the past decade the APA membership increased from approximately 26,000 to 37,000, for an average net gain of about 1,000 members a year. It is apparent, however, that this growth, related in part to the increase in medical students choosing psychiatry (following the 1980 recruitment conference and related efforts) and to our success in recruiting Members-in-Training, has begun to level off. Only Areas I and VII registered gains in membership in 1991-1992. We have engaged in a number of recruitment efforts aimed at women psychiatrists and child psychiatrists who have never been members. We continue efforts to recruit nonmember ABPN diplomates as well. We have completed the data analysis for the 1990-1991 annual census of residents in psychiatry. The number of residents stabilized at almost 6,000, and 681 medical students are members. Analysis of the members who have been dropped demonstrates overrepresentation in some areas, i.e., certain district branches have a higher proportion of drops/resignations than their proportion of membership warrants. Additionally, the largest number of Members-in-Training who were dropped were in their third year; at that time the Members-in-Training who were dropped had never paid dues. We plan to investigate this group of 100 residents in more detail. For General Members, drops tend to take place at times of graduated dues increases, with a peak at year 9. The rate of dropped members who return is low, and so careful attention to retention is needed.

Our studies of member retention (at all levels) have emphasized the importance of the district branch dues structure in membership stability. We also recognize that some areas of the country (e.g., Area VI) are experiencing a "graying" of the membership, with increasing numbers being elevated to Life status, such that district branches continue to provide costly services but without the dues income base to support them. We applaud the work of the Committee on Membership and the Ad Hoc Committee on Membership and Fiscal Planning to develop a proposal for lump sum dues payments, which benefit both the Association and the membership. As of this date, 60 members have used the lump sum national dues payment mechanism. We also appreciate the leadership of the Committee on Membership in considering taking on the functions of producing a new member directory.

Although we have only the initial results of the 1992 National Resident Matching Program, these data indicate that the figures this year for psychiatry will be down considerably from last year. Family medicine and internal medicine apparently are essentially unchanged from last year, and there are increases in emergency medicine and the surgical specialties. In 1992, 526 U.S. seniors matched in psychiatry, down from a high of 745 in 1988 and compared to 641 in 1991. The initial total for U.S. and non-U.S. students matching this year was 695, compared to 786 in 1991. We also are concerned about the impact of limited funding in academic departments of psychiatry and how that affects medical student education and recruitment. Recruitment and medical student education will be a high-priority focus for our educational components this year. The APA census suggests that psychiatry residents have greater satisfaction with their field; considerably fewer residents transfer from psychiatry to training in other specialties. This information is confirmed by an AMA survey that counts psychiatrists among the most highly satisfied practitioners. Residents demonstrate interest in combined residencies and in postresidency subspecialty training. The residents themselves are bright and articulate and bring a special vitality to the Association.

Under the leadership of the American Association of Directors of Psychiatric Residency Training, APA is participating in a working conference on recruitment that was held in Chicago. We reviewed the manpower data, the results of several studies, and the recommendations from the 1980 conference on manpower and recruitment.

We also appreciate the special attention and support provided to residents through the Office of Education and, in particular, the efforts of Ms. Rosalind Keitt in coordinating activities and components addressing resident issues. This work is increasingly demanding and complex, given the growth of resident members in the Association and their increased presence in the governance structure. This year marked the fourth year of having both a Member-in-Training Trustee and Member-in-Training Trustee-Elect on the Board of Trustees, as well as significant active resident participation in the Assembly and Area councils. A component for/on young psychiatrists interacts with its companion component of young physicians in the AMA, as well as addressing the particular needs and issues related to the practice of younger psychiatrists. The retention of residents after training is quite good, and the Board of Trustees demonstrated awareness of special issues for this population by adopting a graduated dues schedule for the first years after residency training.

The Office of Education coordinates the review of nominees for the APA Dista Resident Research Award and the APA Wisniewski Young Psychiatrist Award. We continue to be impressed by the quality and sophistication of the applicants and their projects. The staff also has been developing a host of efforts aimed at medical student information and recruitment. Staff and members participated in the annual meetings of the American Medical Student Association and the National Student Medical Association this year.

The Office of Education works with district branches and other organizations to ensure that educational programs are well planned and organized. We also are meeting with district branch representatives to address the increasingly demanding requirements of the Accreditation Council for Continuing Medical Education for joint sponsorship, to ensure that there are ways for these branches to participate in the formal continuing medical education process. There has been considerable effort to develop self-learning and self-study materials, as well as formal learning opportunities. Most noteworthy has been the Psychiatric Knowledge and Skills Self-Assessment Program (PKSAP). Participants appreciate the opportunity to undertake a com-

prehensive review of their knowledge and to engage in remediation at their own pace and in the location of their choice. The program is seen as especially useful in preparation for ABPN examinations. It is anticipated that it will be part of a proposed recertification process (in the next century!).

One of our most effective initiatives in the public sector is the State/University Collaboration Project, developed by Drs. Talbott and Robinowitz. Funded by the Pew Memorial Trust, the project is co-sponsored by the National Association of State Mental Health Program Directors, the American Association of Chairmen of Departments of Psychiatry, the American Association of Directors of Psychiatric Residency Training, the American Academy of Child and Adolescent Psychiatry, and APA. Its focus is to strengthen collaborative efforts involving education, research, and recruitment and retention of psychiatrists, and the ultimate goal is a positive impact on patient care. It is an important aspect of our efforts to strengthen care in the public sector and to assist psychiatrists who work there.

In the past 2 years, under the superb staff direction of Ms. Ruth Pitlick, the State/University Collaboration Project has sponsored seven regional workshops, provided technical assistance through consultations to more than two dozen state mental health systems and academic departments of psychiatry, and presented awards to programs demonstrating model or exemplary collaboration efforts.

We urge universities and state mental health systems to request free on-site consultations on how specifically to improve their collaborative activities and effect recruitment and retention of psychiatrists in the public sector. These efforts have assisted in consciousness raising nationwide, as well as specific improvements in local function and collaboration. Plans are now under way to expand the effort to include other mental health professionals as well.

Under the leadership of Dr. Robinowitz and with direction and support by Ms. Carol Svoboda, the AIDS Education Project has provided comprehensive programs on the biopsychosocial aspects of AIDS—focusing on prevention and early intervention in addition to long-term treatment of neuropsychiatric and psychosocial aspects of HIV disorders. Conferences have focused on policy issues and emphasized participatory interaction of attendees with faculty and the active involvement of persons with AIDS and HIV disorders. The project's steering committee, under the leadership of Dr. Stuart Nichols, has served as primary faculty and has completed work on the latest edition of the *AIDS Primer* and the videotape "Dealing With AIDS" (copies of which are available on request). Much appreciation has been extended for APA leadership and educational efforts in this important area; the project has reached over 7,000 psychiatrists and other health and mental health professionals.

We have begun liaison activities with APA district branches, medical societies, mental health departments, and existing AIDS education centers to develop resource materials (including curriculum outlines, audiovisual materials, bibliographies, and reference materials); identify AIDS trainers; disseminate information; and mount educational programs. Staff has also used district branch newsletters, *Psychiatric News*, and *Hospital and Community Psychiatry* as vehicles for garnering support for project activities. Surveys were disseminated to 2,000 APA members who expressed interest in AIDS-related activities. Data are being collected to identify regional experts, researchers, educators, and clinicians. The information will be compiled for a resource directory.

The AIDS Education Project has begun collecting materials (participant training manuals, educational guides, audiovisuals) from individuals and groups across the country on the chronically mentally ill, substance abusers, women, children and adolescents, and ethnic minority populations. Staff is currently organizing, reviewing, and/or modifying this material in preparation for review by members of the steering committee, the Commission on AIDS, and selected training consultants. The project is working collaboratively with the American Psychological Association on this activity.

The January 1992 issue of the *American Journal of Psychiatry* was the first to be produced entirely with the desktop publishing system. A comparison of costs for composition (typesetting and page makeup) for the January 1991 and January 1992 issues showed a substantial decrease in expenditures. For the January 1991 issue the average cost per page for composition was \$41; for the January 1992 the average cost per page was \$9. At an average of 160 pages per issue, the *Journal*

should see composition costs reduced by about \$5,000 per issue. We will continue to investigate ways to increase efficiency and lower cost.

I would like to express my gratitude to Mr. William Baxter, our Librarian, for the consultation and assistance he has provided staff in other organizations. At this time of fiscal constraints and heavy workloads, the contributions of staff have been remarkable and highly valued. Mr. Baxter has spearheaded efforts to raise funds for the new Rare Books Room. We have received several significant donations, including a copy of the *Malleus Maleficarum*, published in 1584, during the Papacy of Innocent VIII. We also have begun to develop an on-line catalogue. The Librarian serves as staff liaison to the Ad Hoc Committee to Plan for APA's Sesquicentennial and coordinates staff and member efforts with the Committee on History and Library. We are well into the planning process for 1994; activities are under way for both the annual meeting in Philadelphia (where the founding, 50th-anniversary, and centennial meetings were held) and the Institute on Hospital and Community Psychiatry.

The American Psychiatric Foundation is continuing its organizational development, under the leadership of Dr. Elissa Benedek, Interim President, and Dr. Robinowitz, who serves as Executive Vice-President. Contributions have been made to the APA Library and Division of Public Affairs. Levels of recognition of member and corporate funding have been established. We very much appreciate the individual support provided by the Board and past Presidents; 100% of the Board members, including the resident members, have contributed. This show of support will be especially useful in our external fund-raising efforts. The foundation also is considering ways to use the APA Life Members/Fellows as a support group. I am pleased with its progress in such a brief life span and am anticipating its further support of many important Association efforts.

We are very pleased with the continued development of the Office of Information Systems. Under the leadership of Dr. William More, we have implemented innovative approaches to information services for our members. Our ability to communicate, as well as collect and retrieve information, has expanded immensely. We are very proud of the ongoing routine work of the Association regarding member communication, dues billing, accounting, and financing. Dr. More, who is nationally recognized as a medical statistician, has been an excellent resource in our information generation and data analysis. He bridges the enormously complicated demands of the financial and other aspects of our needs in a creative and supportive manner. We believe that in the future communication and information will be an increasingly important base of our function.

This year marked the 10th anniversary of the American Psychiatric Press, Inc. (APPI). In its first decade, APPI has had spectacular growth, providing outstanding scientific information to the profession and the public, and has become the premier publisher of psychiatric books. APPI has recently initiated publication of five journals, covering the important topics of education, addictions, neuropsychiatry, psychosomatic medicine, and psychotherapy. Congratulations are due Dr. Carol Nadelson, Editor-in-Chief, Mr. Ronald McMillen, General Manager, and staff for their outstanding achievements. APPI has fulfilled three important functions: bringing the best authors and writing to print, providing the best information on topics important for the profession and the public, and generating income to support APA priority activities.

I am most gratified by the creative leadership and energy shown by past President Dr. Carol Nadelson as APPI's Editor-in-Chief. In the past year she has been extremely active not only in broadening and strengthening the ongoing work of APPI but also in outreach to develop strong working relationships with potential authors in this country and abroad. The APPI Editorial Board has been broadened to include experts in a variety of clinical areas. APPI's staff work in expanding our foreign markets has resulted in new professional and business alliances plus greater opportunities. In its 10 years of existence, APPI has become well recognized and highly regarded in the publishing industry. Not only does it have a competitive edge in psychiatric publications, as evidenced by the content of book reviews and by sales volume, but its products also provide an opportunity for scientific education and negation of some of the stereotypes about psychiatry and psychiatric patients.

As a result of a copyright exchange between APA and WHO, APPI will be a major distributor of *ICD-10* in the United States. The "Blue

Book," *ICD-10*, chapter V, on mental and behavioral disorders, will make its first appearance in the United States at the APA annual meeting. The complete *ICD-10* will follow shortly. As a Publishing Partner in Health with WHO, APPI will make available other WHO publications related to psychiatry.

As part of our planning for the World Psychiatric Association meeting in Rio de Janeiro, I am pleased that Drs. Nadelson and Jorge Costa e Silva have agreed to edit an international update, to be published by APPI. This represents a good blend of our interest in international and multicultural topics with the expertise provided by APPI.

Deserving of special recognition are the sustained, remarkably high-level contributions of Mr. Joel Klein. He and his colleagues have done much to support our efforts. We were saddened at the dissolution of the law firm Onek, Klein, and Farr last summer but relieved to retain Mr. Klein's expertise on the Commission on Judicial Action. I will touch on his work on professional liability at a later point. Mr. Klein has been a valued friend as well as counselor through a number of difficult and thorny decision points. Since last summer we have worked primarily with Ms. JoAnn Macbeth, formerly of Onek, Klein, and Farr, now with Crowell and Moring, a full-service law firm. She and her colleagues have been extraordinarily helpful in a wide range of activities related to our business and policy efforts, especially in the work with our ethics procedures. Last year Dr. Hartmann appointed a committee of two, Drs. Benedek and McIntyre, to review our legal needs and make recommendations for the future. In March the Board adopted their recommendation to name Ms. Macbeth as APA legal counsel, continuing our appellate work with Mr. Klein. APA will be well served.

For our insurance program to be successful and meet members' needs, we must constantly deal with the interface and conflict between functioning as a member organization and as a business. While we have to be sensitive to all of the issues and problems practitioners have in dealing with threatened liability, we also have to base the program on a sound fiscal footing and avoid adverse selection. We do offer the best program for meeting members' needs and have more provisions for member choice and control in case settlement. Unlike most commercial carriers, we do not cancel coverage on the basis of suits or claims made. Further, "profit" goes back to the membership in the form of lower premiums, rather than to stockholders. We also are offering on a pilot basis a claims-made policy that may be useful for younger members just beginning practice or those who plan on a stable practice for some time.

Ms. Elizabeth Thomas and Ms. Dara Schumaier developed a strong working relationship with Professional Risk Management Services, Inc. (PRMS) and have been extraordinarily helpful in addressing and solving problems of communication and information. Through their efforts and those of Mr. Rich Feeley, our staff insurance and financial consultant, the number and intensity of insurance-related complaints have fallen considerably.

We have been fortunate to have such effective staff support for our insurance program. Ms. Macbeth, Mr. Klein, and Dr. Robinowitz have devoted much energy to its good functioning and success. Additionally, Dr. Alan Levenson has provided extraordinary leadership, time, and energy to ensure the best possible program and outcome. We also appreciate the contributions made by the many members involved in the committees addressing insurance issues. Their efforts have been vital to our members' practices.

Business ventures demand both substantive knowledge of issues affecting our members and their practices and a sound fiscal structure. Dealing with tight budgets, the recession, and the leveling off of income while ensuring prudent planning for the future financial strength of the Association has been a monumental effort, demanding considerable member and staff coordination and proactive planning.

This year we have focused extensively on budget and financing. Over the past decade we increasingly used outside funds (nondues income) to support new and high-priority projects. The termination of our Quality Assurance Program brought with it not only the costs of termination but also a loss of outside income. This is reflected in the lack of funds for new projects and also brings the realization that increased funding is needed just to maintain the inflationary growth of ongoing programs. In response to members' concerns, dues for 1992, which represent some 40% of the operating budget, were held to an increase paralleling inflation. The recession has had an effect on

both income (e.g., from advertising sales) and the costs of doing business (e.g., travel, postage). It also is felt in the increased number of members requesting dues relief.

Consequently, the 1992 budget is not able to maintain 1991 programs at the level of inflation or to fund and initiate new programs. We are pleased that we ended 1991 with a balanced budget and a very small surplus. Extremely careful monitoring of expenditures and attention to generation of funds and use of resources was needed to effect this outcome. In particular, the *American Journal of Psychiatry*, the annual meeting, and APPI were noteworthy sources of income. To continue in this direction will demand care on the part of staff and members in monitoring expenses and generating income.

We have improved cost-effectiveness through integration and consolidation of efforts and careful review of priorities and expenditures. With the assistance of Mr. Feeley, we developed a model to analyze monthly expenditures according to seasonal variation, since our expenses do not occur at a regular monthly rate but, rather, in predictable response to events on the Association's calendar each year. We continue to monitor departmental expenditures closely to ensure compliance with this year's budget and fiscal state. Positions are almost always frozen when current staff depart, supply and equipment purchases are curtailed, and travel also is severely limited. The new travel contract was designed to provide savings, as is our increased use of desktop publishing. Morale is an issue, as we curtail some resources without limiting activities. At the same time, we want to avoid layoffs. Staff and members alike will feel the pinch as we attempt to streamline efforts further, and I recognize that the leadership will continue to be approached by many members requesting support for programs and activities they consider of highest priority. The next few years will be a time of careful priority setting, and the results of our fiscal actions will be vital to the long-term health and function of the Association. We have been most fortunate to have Dr. Donald Scherl as chairperson of the Budget Committee. His wisdom and careful attention to long-term, as well as immediate, issues is remarkable. He and staff have worked closely with APA Treasurer Dr. Mary Jane England and with Board and Assembly leaders on financial planning and implementation, ensuring income for the Association and regulating expenses. I especially appreciate the efforts of Drs. Robinowitz and White, Comptroller Mr. Robert Milanicz, and Mr. Feeley in what represents a longer-term strategic financial planning endeavor. They have done an excellent job not only in planning and execution but also in dealing with the many individual needs generated by fiscal restraints.

As part of the 1993 Presidential theme and directions set by President-Elect English, we have had several meetings to address issues related to access to, and delivery of, services in the public sector. I have had some very gratifying contacts with Dr. Richard Surles, Commissioner of the New York State Office of Mental Health. He has expressed his strong support for the role of psychiatry in public mental health settings. Dr. English is planning a small invitational working conference to begin a process to address these topics and to consider

issues of professional values, development, and function, as well as patient care, in the context of economic constraints and environmental forces that will be at play in the coming decade. We have obtained financial support for the initial working conference from NIMH and from Dr. Alexander Gralnick, Psychiatrist-in-Chief at High Point Hospital in Port Chester, N.Y.

No report would be complete without some comments about staff in my office, whose work has been exemplary. Mr. David McClanahan has contributed strongly to the day-to-day smooth functioning of my office. Ms. Katherine Chambless has been a marvelous addition to the team. Ms. Sandy Hazen has been invaluable in so many areas, including production of this report. We were delighted at the return of Ms. Emma Wilkins to our staff; her willingness to assist whenever and wherever needed is a model for us all. Dr. Robinowitz also has been pivotal in this integrative effort, which, in my judgment, shows APA at its working best. Further, Dr. Robinowitz has consistently taken on increasing responsibilities in all areas of Association functioning and has performed magnificently. As far as I am concerned, our working partnership in the day-to-day and long-range management is excellent.

Of vital importance is the presence of a largely behind-the-scenes staff member who takes major responsibility for making it all happen. Ms. Carol Davis oversees the functioning of my office and all of its related activities, while at the same time maintaining major staff support responsibility for the demanding work of the Ethics Committee, the Ethics Appeals Board, and our involvement with the AMA. She has a special ability to develop and implement planning processes and is an extraordinarily knowledgeable and sensitive resource. The nature of her work is such that she rarely receives public attention or recognition, yet her contributions are invaluable and she has won the trust and respect of us all.

Comments about "the best in APA" are a good link to my belief that we have been extremely fortunate in our choice of leaders. Our President, Dr. Lawrence Hartmann, has been outstanding; his knowledge, vision, concern, and effectiveness have had a major impact on our functions and our future. Our Speaker, Dr. Thomas Pfahler, also deserves special recognition. His sensitivity to and knowledge of Assembly moods, directions, and needs and his remarkable ability to deal with administrative issues while working closely with members and staff have made him especially effective for the Assembly and the Association. It has been a privilege to work with all of our members this year toward a stronger and more effective APA, and I anticipate an excellent alliance with our incoming President, Dr. Joseph English, and with the next Speaker, Dr. Ronald Shellow, and all the other APA members who serve the Association and the field so ably.

Extensive reports on the individual staff departments are available from the Central Office. They attest to the diversity, enormity, and complexity of staff efforts and demonstrate our commitment to strengthening the field and supporting our members and the patients whom they serve. It is a privilege and pleasure to be Medical Director of such a strong and vital organization.

Report of the Speaker

G. Thomas Pfaehler, M.D.

The theme of my Speaker-Elect's report was evolution: the evolution of issues, the evolution of the Assembly, and personal evolution. Diverse issues continue to command the attention of the Assembly. These issues continue to occupy the efforts and resources of APA:

- *Professional liability insurance.* This program has been recently tested in the glare of national media.
- *Quality assurance and APA.* Quality assurance has drifted further from the control of APA, and quality improvement has only appeared on the horizon.
- *American Psychiatric Foundation.* APA must decide whether to commit to outside fund raising under the coordination of its affiliated foundation.
- *Practice guidelines.* Two major guidelines, on eating disorders and major depression, are nearing final approval and publication.
- *CPT-IV.* Confusion still reigns as different geographic areas and fiscal intermediaries provide different rules and interpretations for *Physicians' Current Procedural Terminology*, 4th edition.
- *Managed care.* 1991 has seen progress in confronting firms using abusive and inappropriate methods. *Utilization Management—A Handbook for Psychiatrists* ("Survival Manual") is a great success.
- *DSM-IV.* The DSM-IV, *Work in Progress: Options Book* has been available through the year to provide insight into the process of developing the latest nosological scheme.
- *Recertification.* Continuing to bear down on the membership with time-limited certification just 2 years away, recertification is a pressing issue.
- *Resource-based relative value scale.* APA has been successful at limiting the degree to which the federal government has fallen short of the intent of the law in implementing this system.
- *Active service of minority and underserved populations.* APA continues its struggle to maintain credibility as the umbrella organization for these groups amidst an increasingly pluralistic society with rapidly growing minority groups.
- *Subspecialization.* With the establishment of added qualifications for the most obvious of clinical populations, APA now faces the challenge of possibly saying "no" to petitioners.

Now, with these issues in mind at the end of my term, I wish to accomplish two tasks: first, I wish to state the challenge I see facing APA, and second, I wish to take the opportunity to acknowledge those who have been important to me during this year.

CHALLENGE

Given the breadth and complexity of the issues facing us, we must seriously question whether APA can confront all of them effectively. If all cannot be confronted, a system of priorities is essential. We must make hard decisions regarding the expenditure of resources, the allocation and size of staff, and the satisfaction of some people, occasionally at the expense of others. To be effective in essential areas may require small membership attrition and loss as APA faces, with other large organizations in our society, the necessity of modifying the ideal of being all things to all members.

APA no longer exists in a world that automatically grants favored positions to physicians and other professionals. Increasingly we must earn, and re-earn, our recognition and benefits. We will be increasingly scrutinized in sometimes painful ways, as we were in the "Frontline" program on PBS. The impact on us all of professional misfortune and poor judgment on the part of a few of our prominent members, as demonstrated in recent events, is hurtful and diminishing to our reputation.

The practice of medicine has been regarded by regulators as a busi-

ness for two decades. We must continually tread carefully to avoid damaging our unity by exclusive attempts to preserve our professional identity.

- Which of the issues previously identified deserve the highest priority?
- Will we always be perceptive and courageous enough to take the professional "high road" when attacked or when embarrassed and sullied by the behavior of a few of our own?
- Can we avoid unnecessary and resource-exhausting battles with competing professional groups and government-sized regulators of our practice that could cause us to lose the war of professional survival?
- Can we conceptualize ourselves and what we do responsibly and flexibly enough to permit recognition of the need for change and evolution within the society around us?
- Can we recognize the fact that we and other professionals, such as college professors and public servants, are no longer the masters of the roles we fulfill in society but are increasingly having our roles defined by others—frequently those others who either consume or pay for our services and demand value and quality outcomes?

My year as Speaker has shown me that all of these questions are constantly appearing in the work facing the Assembly. The year has built my confidence that the Assembly can, and does, confront the issues when they arise. For example, it confronts the conflict between those who believe APA should control what roles are acceptable for its members through incentives and disincentives and those who believe we should cooperate with redefinition of our roles while working to exemplify the best of our professional contributions. It confronts the conflict between the need to finance the operations of APA while at the same time requesting members to provide additional personal and financial resources to support educational and special endeavors. The strength to make our negotiations credible, and our challenges of others formidable, requires such resources.

ACKNOWLEDGMENTS

In closing my year I must, as have all Speakers before me, recognize that I am a part of a continuum. I am able to serve the Assembly ably only insofar as I can recognize and use the support and knowledge of those around me. Past Speakers Dr. Edward Hanin, Dr. John McIntyre, and Dr. Gerald Flamm have been available and supportive, often giving me time from their own busy and advancing careers. The Speaker-Elect, Dr. Ronald Shellow, has been available and has provided valuable counsel. His eagerness to assume his own place in the continuum becomes him. It will be a pleasure to pass the gavel to him.

Dr. Lawrence Hartmann has been an easy and steady influence in subtle ways throughout the year. I have discovered in him a source of support of which even he may be unaware.

Mr. Michael Murphy, Ms. Jeanne Robb, Ms. Lea Mesner, and Ms. Elisabeth Fitzhugh from the Office to Coordinate the Board and Assembly are indispensable. This report is perhaps the only thing that does not appear in the literary style of one or another of these valued people. They are our memories, our planners, and, often enough, our encouragement. Michael Murphy will be missed but is also to be congratulated for his promotion.

Finally, the superb staff under the guidance and direction of Dr. Melvin Sabshin continues to serve APA well in private and in public arenas. Mr. Jay Cutler and Mr. John Blamphin, particularly, are willing to advise, to challenge, and sometimes to risk in the service of advancing the values of psychiatry.

I thank, mostly, the members of the Assembly who elected me and provided me with this opportunity to serve. I hope that the personal evolution of which I spoke in May of 1991 has been as evident to them as it has to me.

Last, I recognize my family, who tolerated delays in tasks resulting from my absence, provided rides to the airport (and sometimes home from the airport), and generally encouraged and advised me during the year. Their support was, and is, essential.

Report of the Speaker-Elect

Ronald A. Shellow, M.D.

The Speaker-Elect is expected to report to the Association at the annual meeting. Two factors color my report—pleasure at APA's return to its important goals and altered perceptions resulting from a year in this office.

First, after a period of increased focus on protecting guild interests of members, APA has returned to emphasizing its stated goals: to promote learning and exchange of knowledge, to share appropriate standards and ethics within our specialty, and to be advocates for our patients locally, nationally, and internationally.

The second factor influencing me was my role as Speaker-Elect, assisting the Speaker and cochairing the Joint Reference Committee. Additionally, I continue with committee responsibilities, the Section Council on Psychiatry to the AMA, and district branch work. These activities, which compelled me to be away from my office 20% to 30% of last year, have made a great difference in my solo private practice. Local physicians no longer refer patients to me, I see no hospital patients, and I must more carefully select new psychotherapy patients. I am not available to work in any managed care settings aside from meeting demands of the insurance carriers for some of my outpatients. To fill the gap, I have increased consultations, evaluations, and forensic practice. The combination of these changes has given me a different perspective on organized psychiatry, which leads to the following thoughts. By accentuating our professionalism, the Association is taking steps that help psychiatry better serve our patients' welfare. I am proud of this direction and hope colleagues share my pride.

One of the outstanding contributions of APA, not only to our patients but to all of medicine, has been more accurate diagnosis of psychiatric disorders. To further aid in this critical task, we are in the midst of producing *DSM-IV*. Recognizing its importance, the Assembly has provided substantial input for this project. Each member received, and many commented on, *DSM-IV, Work in Progress: Options Book*. We look forward to the timely publication of *DSM-IV*.

I am personally more involved in production of practice guidelines. T. Byram Karasu and the Task Force on Treatments of Psychiatric Disorders gave our specialty a huge push forward by publishing the four-volume *Treatments of Psychiatric Disorders* several years ago. Building on this start and evolving from recommendations originating in the Assembly, through a steering committee now chaired by John McIntyre, the first guideline is almost ready for publication. The second guideline is near completion, and the next two should be ready later this year. This process can only help improve standards of psychiatric care for people suffering from mental disorders. Other probable benefits of the guidelines include improving relations with other specialties of medicine, easing the burden of professional liability, and assisting in work with parties involved in financing health care. The guidelines project deserves increased support, both for initial publication and frequent revisions. Expanding knowledge in psychiatry demands this.

Our focus on access to health care for psychiatric patients highlights another way in which APA tries to help these patients. While psychiatry is really a small player in the arena of comprehensive health care, too many of our patients have no access to the system

of insured care because of insufficient money, preexisting illnesses that make them "indentured servants" to employers who carry their present insurance, unrealistic present benefits, or managed care agencies that so interfere with the system as to negate their psychiatric benefits. Small player or not, on behalf of our patients APA must continue to work diligently with government, industry, patient advocacy groups, our members, and other interested parties. We continue to educate ourselves about all systems purporting to improve access. Our primary focus, however, should be to attempt in every reasonable way to provide adequate, preferably nondiscriminatory, third-party benefits to those patients. The Assembly has advanced this position to the more executive components of APA: Board of Trustees, Joint Reference Committee, Joint Commissions on Government Relations and Public Affairs, Committee on Universal Access to Health Care, and staff. Emphasis on psychoanalytic concepts in the past may have slanted the profession too far in one direction. Spectacular achievements in biological psychiatry now may be pushing us too far the other way. Prompted in part by Lawrence Hartmann's Presidential theme emphasizing a biopsychosocial perspective, the Assembly asked the Scientific Program Committee to ensure that members have more opportunities to maintain and improve skills in psychotherapy. Additionally, the Assembly has urged caution in isolating "biological" psychiatric illnesses from those which, at this time, are still labeled "purely functional." We must be careful not to abandon any patients who could benefit from psychiatric help.

APA continues to actively promote the welfare of psychiatric patients by trying to improve standards for their care. As part of this effort, we oppose inappropriate extension to nonphysicians of the privilege of prescribing medication or admitting and treating patients in hospitals without supervision. Some psychologists have called this a "turf issue." They are wrong. Instead, it is an issue of proper care for sick human beings. Nonphysicians who are less qualified simply cannot competently care for patients, and, in fact, psychiatrists themselves should seek additional training and education. On behalf of our patients we must try to ensure that utilization management does not interfere with delivery of high-quality, efficient psychiatric care. We must continue to be vigorous in promoting high standards and combating excesses of utilization managers, especially now that the Assembly has given the Board a rational set of prioritized approaches.

APA is the most vigorous of all medical and specialty organizations in promoting high ethical standards of professional conduct. We should be proud of our record and diligent in trying to improve that record. We should also seek methods of ensuring that our public image truly reflects the assertiveness of our work in this regard.

Further, in a time of serious fiscal difficulty APA should continue attempts to preserve funding for research into mental disorders.

APA is one of the most representative medical organizations. In part, this responsiveness to its membership is a product of its governance structure. The Assembly continues to be an important and effective component of that governance. I have been particularly fortunate this year to have been able to work with the Speaker, G. Thomas Pfahler, a man of extraordinary administrative and organizational

skills combined with great patience and creativity. As Speaker-Elect I have also worked closely with President-Elect Joseph English. Joe has outstanding concentration and an innovative, outward-looking vision of our organization. He has been a superb chairperson of the Joint Reference Committee. The three immediate past Speakers of the Assembly—Edward Hanin, Gerald Flamm, and John McIntyre—and Parliamentarian Frederick Gottlieb have been of great help to me with advice, counsel, and hard work whenever asked. Medical Director Melvin Sabshin has, with grace and style, in this time of financial constraint, maintained important aspects of APA's goals for our mem-

bers and profession. The staff of the Office to Coordinate the Board and Assembly, led by Jeanne Robb and including Michael Murphy, Lea Mesner, and Elisabeth Fitzhugh, have been superb in willingly supporting and carrying forward the institutional memory and day-to-day functions of the Assembly, district branches, and other components of the governance structure. Corky Hart, providing staff assistance to the Joint Reference Committee, has played an important role in coordinating Assembly issues in councils and other components. Members of the Assembly of District Branches have given their time, energy, and hard work for all the membership. I thank them all.

Report of the Committee on Constitution and Bylaws

Henry Payson, M.D., Chairperson

The Committee on Constitution and Bylaws this year accomplished its work by mail ballot, and I am indebted to the members of the committee for completing its business so expeditiously. They include Drs. William Spiegel, Richard Thurrell, Walter Shervington, Naomi Goldstein, Alexandra Symonds, and Lee Park, Assembly liaison. The committee was assisted by Ms. Carol Lehmann of staff.

The committee was asked by the Medical Director to review the part of chapter 8.5 (the Bylaw that outlines procedures for referenda) that reads, "For a referendum to pass, at least 40 percent of the total number of members eligible to vote must vote and at least one-third of the total number of members eligible to vote must vote in favor." Given the current wording, it is possible, albeit unlikely, for a referendum to pass without a majority vote. The committee prepared an amendment which stipulates that a majority vote is needed for a referendum to pass.

At its March 21–22, 1992, meeting, the Board of Trustees approved the amendment for reading to the membership at the 1992 annual business meeting and for inclusion in the 1993 ballot. The text of the amendment follows.

At its March meeting the Board also asked the committee to approve an amendment to chapter 10.1 that will allow the name of a member who resigns before an ethics complaint is filed to be reported to the membership and to the National Practitioner Data Bank, if the complaint is filed within 90 days after the member submits the resignation. The committee approved this amendment; the text follows.

PROPOSED AMENDMENTS TO THE CONSTITUTION AND BYLAWS

The following amendments were approved by the Board of Trustees in March and April 1992 for reading to the membership at the 1992 annual meeting. The amendments will be disseminated to the membership not later than Jan. 1, 1993, and will appear on the 1993 ballot. In the text that follows, bold underscoring indicates additions.

Chapter Eight. Privileges and Responsibilities

5. The voting membership may initiate referenda or change an action of the Board by the following procedure: A petition signed by at least 500 voting members shall be submitted to the Secretary by November 15 to be voted on in the mail ballot in the following year. A statement from the petitioners setting forth the reasons for the action, following consultation with the President, Speaker, Medical Director, and legal counsel (including fiscal advice), and a statement from the Board shall accompany the ballot. For a referendum to pass, at least 40% of the total number of members eligible to vote must vote and at least one-third of the total number of members eligible to vote must vote in favor. **In addition, it requires a majority vote.** A referendum overturning an action of the Board shall be binding, except that the action may be reinstated by a two-thirds affirmative vote of the members of the Board eligible to vote and by a two-thirds affirmative vote of the members of the Assembly Executive Committee eligible to vote. A Board action to reinstate may be taken only at a regularly scheduled meeting occurring no sooner than one month after the meeting at which the referendum was certified. Certified referenda other than those overturning an action of the Board must be acted on by the Board with all deliberate speed.

Chapter Ten. Ethics Complaints and Disciplinary Procedures

1. Complaints charging members of the Association with unethical behavior or practices shall be investigated, processed, and resolved in accordance with procedures approved by the Assembly and the Board. The name of a member who resigns during an ethics investigation may be reported to the membership. **The name of a member against whom an ethics complaint is filed within 90 days after the member submits a resignation may be reported to the membership and to the National Practitioner Data Bank.**

Report of the Committee on Membership

Aron S. Wolf, M.D., Chairperson

The Committee on Membership met Nov. 5–8, 1991, in Washington, D.C. Present were Drs. Aron S. Wolf (chairperson), Jack W. Bonner III, Fernando J. Cabrera, Siobhan Coomaraswamy, Lois B. Fuller, Rodrigo A. Munoz, A. Granville Tolley, and Michael J. Vergare (consultant); Ms. Elizabeth Thomas, Director, Office of Membership; and Office of Membership staff. Guests present were Dr. Melvin Sabshin, Medical Director; Dr. Carolyn B. Robinowitz, Senior Deputy Medical Director; Dr. Harold A. Pincus, Deputy Medical Director; Dr. William More, Director, Office of Information Systems; Mr. Thomas Dial, Assistant Director for Research Studies; and Dr. James R. Rundell, President of the Society of American Military Psychiatrists.

The committee held a joint meeting with the Assembly Committee on Membership Recruitment and Participation on Friday, Nov. 8, 1991.

Certain information contained in this report has been updated since the November meeting.

MEMBERSHIP DEVELOPMENT

The total membership as of April 1, 1992, was 37,512, which reflects a net gain of 361 in 1991. The net gain for 1991 is below the net gain of 710 for 1990, in part because of the stable numbers of medical students entering psychiatric residencies, which has resulted in fewer new members, and in part because of increased economic pressures on members, who may find membership dues less affordable than in the past.

1991 was the first year in which annual membership termination for nonpayment of APA dues took place in June rather than December. Losses due to membership termination for nonpayment of APA national dues were not as severe as anticipated but were in line with the organization's experience in previous years. Losses were kept to a minimum largely because of extensive personalized correspondence between the Office of Membership and members facing termination.

The distribution of members among the membership classes from 1988 to 1992 can be seen in table 1. A summary of percentage changes in membership by Area from 1986 through December 1991 is given in table 2. Five of the seven Areas showed net losses for 1991. The downward trend for 1990 and 1991 requires serious consideration by everyone in the APA leadership.

It is important to note that table 2 reflects not only annual terminations but also the removal of Medical Student Members from Area and district branch membership (as of July 1, 1991, medical students were enrolled as APA members only). As of April 1992, Medical Student Members comprise 2.0% of the membership overall. The new one-time-only \$25 fee seems to have been well received; during 1991 medical student enrollments increased slightly in September and October over previous months.

As of April 1, 1992, the 5,823 Members-in-Training plus the 745 Medical Student Members represent a substantial 17.5% of the total membership. Members-in-Training continue to be the greatest source of new General Members. It is believed that close to 80% of all psychiatric residents are members, and increased emphasis on recruiting the remainder is a priority. The proportion that had been used previously was 90%; an appraisal of the advancement data accounts for the difference. The number of new members who are enrolled as General Members is still decreasing, while the proportion of those who become General Members by advancement has grown steadily. Table 3 shows General Member enrollment versus advancement from Member-in-Training for the past 8 years.

In October 1991 the Office of Membership sent 2,277 letters to all Members-in-Training who had held that status for 5 or more years, asking them to initiate advancement of their membership or notify the office of any continued training they have undertaken. Traditionally, the district branches have been provided with rosters of their members who may need to advance so that the branches can contact

these members. The Office of Membership hopes that by contacting members directly advancements can be accelerated and some of the paperwork burden at the district branch level can be relieved (some district branches do not have staff but rely on members to handle membership transactions and paperwork).

In October 1991 each member whose mailing address fell outside the jurisdiction of the district branch to which he or she belonged was mailed a letter asking the member to initiate the transfer process. After that initial mailing, on a monthly basis the Office of Membership began sending letters to members whose changes of address indicated a need to transfer district branch affiliation.

Table 4 shows membership transactions for 1991, and table 5 summarizes the transactions for 1982–1991. Membership reinstatements were up in 1991; more members were reinstated during 1991 than during 1990 (56 Members-in-Training and 170 General Members were reinstated in 1991, compared to 36 and 123, respectively, in 1990). This may be due in part to the dues amnesty that had been in effect for 1990 and 1991 (members owing more than 2 years' dues before 1988 paid only the more distal year's dues to be reinstated).

In addition to a successful reinstatement campaign, during 1991 the Office of Membership contacted 91 new diplomates of the American Board of Psychiatry and Neurology (ABPN) who had never been APA members about joining APA. Another recruitment project involved contacting over 1,000 female psychiatrists who had not previously belonged to APA; of 1,045 who received letters and applications, 121 became members of APA and their local societies (91 as Members-in-Training and 30 as General Members). This represents 11.6% of those contacted, which is a very high return for this type of recruitment effort (2%–3% is the average return).

The schedule for APA national dues was revised for 1992. Dues for General Members now increase more gradually, from 30% of full dues during the first year of General Membership to full dues in the 8th year of General Membership.

During 1991, 370 members resigned from APA, 526 members were dropped for nonpayment of dues, 174 members were dropped by their district branches (and therefore also by APA), and 152 Medical Student Members were dropped because their membership had expired by virtue of their graduation from medical school.

There have been staff changes in the Office of Membership since the committee's last meeting. Ms. Elizabeth Thomas was promoted to Director after former Director Marta De Lalla, Ph.D., resigned to return to Argentina. Also, Ms. Dara Schumaier, who was the Coordinator for Recruitment/Retention, was promoted to Special Assistant to the Senior Deputy Medical Director (Dr. Carolyn Robinowitz). Mr. Michael Murphy was promoted from the Office to Coordinate the Board and Assembly to Assistant Director of the Office of Membership, and Ms. Susan Kuper was promoted from the Office of Psychiatric Services to Coordinator for Recruitment/Retention in the Office of Membership.

FELLOWSHIP

The Committee on Membership received 228 nominations submitted by 58 district branches for elevation of members to Fellowship. The five requests for waivers of the 2-year waiting period or the 8-year General Member requirement were all denied, and thus the committee reviewed the remaining 223 nominations. The approval rate was 81.6%: 182 candidates' nominations were approved, and 41 were deferred. The committee commends the district branches for their fine work in ensuring that the nomination materials submitted were complete, thus ensuring a fair evaluation of the candidates.

The issue of Fellowship denial at the branch level was discussed in depth by both membership committees. This issue arose from a review of one member's concern that his nomination had been blocked by

TABLE 1. Members in Each Class, 1988–1992

Membership Class	Jan. 1, 1988		Jan. 1, 1989		Jan. 1, 1990		Jan. 1, 1991		Jan. 1, 1992		April 1, 1992	
	N	%	N	%	N	%	N	%	N	%	N	%
Dues-paying	28,091	81.9	28,250	80.4	28,917	79.9	29,263	79.3	29,332	78.7	29,526	78.7
Member-in-Training	5,366	15.6	5,594	15.9	5,856	16.2	5,760	15.6	5,892	15.8	5,823	15.5
Associate Member	302	0.9	263	0.8	228	0.6	192	0.5	171	0.5	169	0.5
General Member	18,653	54.4	18,847	53.6	19,299	53.3	19,791	53.6	19,801	53.1	20,073	53.5
Fellow	3,770	11.0	3,546	10.1	3,534	9.8	3,520	9.5	3,468	9.3	3,461	9.2
Dues-exempt	5,607	16.3	6,260	17.7	6,570	18.2	6,887	18.6	7,266	19.5	7,241	19.4
Life status	4,157	12.1	4,785	13.6	5,032	14.0	5,285	14.3	5,588	15.0	5,553	14.8
Life Member	1,365	4.0	1,700	4.8	1,844	5.1	2,007	5.4	2,202	5.9	2,186	5.8
Life Fellow	2,753	8.0	3,033	8.6	3,133	8.7	3,215	8.7	3,318	8.9	3,299	8.8
Life Associate	39	0.1	52	0.2	55	0.2	63	0.2	68	0.2	68	0.2
Other	1,450	4.2	1,475	4.1	1,538	4.2	1,602	4.3	1,678	4.5	1,688	4.6
Inactive Member	682	2.0	713	2.0	745	2.1	777	2.1	805	2.2	805	2.2
Inactive Fellow	132	0.4	119	0.3	115	0.3	109	0.3	107	0.3	106	0.3
Corresponding Member	350	1.0	362	1.0	393	1.1	425	1.2	473	1.3	482	1.3
Corresponding Fellow	222	0.6	220	0.6	228	0.6	235	0.6	235	0.6	237	0.6
Distinguished Fellow	30	0.1	30	0.1	28	0.1	27	0.1	26	0.1	26	0.1
Honorary Fellow	34	0.1	31	0.1	29	0.1	29	0.1	32	0.1	32	0.1
Subtotal	33,698	98.2	34,510	98.1	35,487	98.0	36,150	97.9	36,598	98.2	36,767	98.0
Medical Student Member	608	1.8	658	1.9	721	2.0	768	2.1	681	1.8	745	2.0
Total	34,306	100.0	35,168	100.0	36,208	100.0	36,918	100.0	37,279	100.0	37,512	100.0

TABLE 2. Percent Change in Membership by Area, 1986–1991

Membership Group	% Increase in Membership					
	1986	1987	1988	1989	1990	1991
Area						
I	6.2	3.5	5.5	4.9	1.8	1.0
II	3.2	1.8	0.9	0.1	1.0	-1.7
III	4.3	4.3	1.4	3.6	2.6	-1.2
IV	6.4	2.6	2.1	2.5	1.2	-3.3
V	5.3	5.5	4.7	3.9	4.0	-0.1
VI	1.8	0.7	2.1	2.9	-0.1	-2.7
VII	6.8	3.9	2.8	5.8	3.2	2.9
Total	4.8	3.2	2.8	3.1	2.0	-1.0
At-Large Members	0.9	-0.5	-2.3	-0.1	0.5	1.6
Total	4.6	3.0	2.5	3.0	2.0	1.0

TABLE 3. General Members Gained From Enrollment and Advancement, 1984–1991

Year	Total New General Members	Enrolled	Advanced From Member-in-Training	
			N	%
1984	1,027	457	570	56
1985	1,121	480	641	57
1986	1,107	395	712	64
1987	1,105	285	820	74
1988	1,185	263	922	78
1989	1,285	215	1,070	83
1990	1,408	182	1,226	87
1991	1,080	180	900	83

the district branch, and it was revealed that no specific appeal mechanism appears to be in place. Procedural and legal issues will be referred to appropriate staff for clarification, and the committees will discuss this matter again at their joint meeting in May 1992.

The committees refined and clarified the guidelines for election to Fellowship to be used from 1992 onward. One of the purposes was to deemphasize certain characteristics, such as board certification, while encouraging public sector service (as requested by the Consortium of Chairpersons of APA Public Psychiatry Components) and socially responsible medical and mental health activities that are unremunerated.

Finally, the committee continued discussions regarding ethics and revocation of Fellowship of members who are under suspension. Committee members continued to have unanswered questions about how suspension relates to the honor of Fellowship. The committee will continue its dialogue with the Ethics Committee and will ask for further clarification from that committee about the relationship between suspension and Fellowship. The central issues are whether Fellowship is primarily a member class, a one-and-all-time honor, or an acknowledgment of both past and present honorary status within APA.

SELECTED MEMBERSHIP ISSUES

Reduced Dues

A request for reduced dues for academic psychiatrists was reviewed by the Committee on Membership. The committee believes that the

current dues relief options available to members adequately meet the needs of those who are unable to meet their dues obligations; it was also noted that several dues billings are sent throughout the year, enabling members to make partial payments. The committee also discussed correspondence from residents regarding the level of district branch dues. The committee strongly recommends that the district branches exercise considerable restraint in setting dues for residents.

Dues Late Fee or Discount

The committee continued its review of information, including an opinion from legal counsel, about the use of late fees or discounts connected to dues payments. The committee will solicit further information exploring the feasibility of offering a prompt-payment discount (including a cost-benefit study and questions to district branches who use discounts and/or late fees about their experiences), keeping in mind the large number of members who already pay their dues promptly. It was felt that charging a late fee would be counterproductive because it may be viewed as punitive.

Recruitment for Western Canada District Branch

The committee reviewed correspondence between the President of the Western Canada District Branch and the Office of Membership addressing strategies for recruiting (and retaining) members for this district branch. The committee suggested that the recruitment problems may be geographically based. It believes that the Western Canada District Branch might investigate the benefits of subdividing, forming

TABLE 4. 1991 Membership Transactions

Transaction ^a	N
Gains	1,847
New members	1,621
Medical Student Members	311
Members-in-Training	1,089
General Members	180
Corresponding Members	32
Corresponding Fellows	6
Distinguished Fellows	0
Honorary Fellows	3
Reinstatements	226
Medical Student Members	0
Members-in-Training	56
General Members	170
Fellows	0
Losses	1,486
Resignations and drops	1,222
Resignations from APA	370
Drops for nonpayment of APA dues ^b	526
Other APA drops	0
Drops/resignations from district branches and thus from APA	174
Medical Student Members whose membership expired	152
Verified deaths	264
Net gain	361
Changes in membership status	1,750
To Member-in-Training from	184
Associate Member	1
General Member	17
Medical Student Member	166
To General Member from	905
Member-in-Training	900
Inactive Member	4
Associate Member	1
Return to Fellow from Inactive Fellow	1
To Corresponding Member from General Member	17
To Corresponding Fellow from Corresponding Member	1
To Fellow status from	182
General Member	179
Life Member (to Life Fellow)	3
To Life Status from	460
Fellow (to Life Fellow)	179
General Member (to Life Member)	196
Life Member/Fellow (to 50-Year Life)	74
Associate Member (to Life Associate)	11
Transfers between district branches	1,082
Recommendations for deferral or denial of Fellowship status ^c	46
Deferral of transfer of General Member to Fellow	41
Denial of waiver of 2-year waiting period for renomination for Fellowship (not reviewed)	4
Denial of waiver of 8-year General Member requirement	1
Requests for dues relief or Inactive status	391
Approved	319
Dues waivers	153
Dues waivers for reinstatement	10
Dues waivers to reach Life status	22
Reduction of dues	55
Refund of dues	1
Extension/deferral of payment	2
Transfer to Temporary Inactive status	14
Transfer to Permanent Inactive status	62
Deferred or denied	72
Temporary Inactive status	1
Permanent Inactive status	7
Dues waivers	18
Dues waivers to reach Life status	2

TABLE 4 (continued)

Transaction ^a	N
Deferred or denied, cont'd	
Reduction of dues	7
No action pending district branch recommendation	37

^aIn addition, 6,093 address changes were processed; this total may be underinclusive since it reflects only one change per member and multiple changes are not reported.

^bAnnual drop and miscellaneous drops throughout the year.

^c228 nominations submitted.

a new "prairie" district branch consisting of Manitoba, Alberta, and Saskatchewan. A first step in this process might be for the Western Canada District Branch to identify members in its three provinces east of the Rockies who might be possible leaders (should the branch subdivide). The outcome of this discussion was shared with the president of the Western Canada District Branch.

Annual Statement From Members

A request was received from a district branch asking if the APA Bylaws prohibit asking a member if she or he has been convicted of any ethical violation, has been found liable in a malpractice suit, or has had hospital privileges revoked or rescinded. APA legal counsel was asked for an opinion on requesting members to sign an annual statement on these matters. Although neither counsel nor the committee found any problem with the branch's soliciting this information from its members, the committee felt strongly that a number of questions raised by legal counsel should be carefully considered by the district branch before it implements such a procedure. The branch did not specify how it intends to use the information. Counsel stated in the opinion that its use may well contravene—at least implicitly—provisions of both the Bylaws and the "Operations Manual of the Board of Trustees."

Dual Membership Requirement

The committee reviewed correspondence from several members who objected to belonging to their local district branches. The committee reviews similar correspondence each year; it reiterates the value and importance of maintaining the dual membership requirement and will not grant exceptions to this requirement.

Osteopathic Physicians

At the request of both membership committees, the Committee on Graduate Education was asked to review the accreditation standard of the American Osteopathic Association as an initial step in determining eligibility for General Membership (General Members must have completed a psychiatry residency training program approved by the Accreditation Council for Graduate Medical Education [ACGME]). The Committee on Graduate Education foresaw a conflict in reviewing and sanctioning a second accreditation track and was reluctant to take a position on this issue. The membership committees reached the conclusion that at this time it is not possible to include formally in the APA membership psychiatrists with osteopathic psychiatry residency training. Both committees suggested that district branches interested in including osteopathically trained colleagues in continuing medical education and other branch activities develop local-level invitational mechanisms to maintain contact with them.

Lump-Sum Dues

The option of paying APA national dues in a lump sum currently is being offered to members who are 40 years old or older. Although this option is new, 62 such payments had been received as of April 1992. In response to the interest of a member younger than 40, APA's financial consultant will be asked to calculate the appropriate lump-sum amount for members aged 35–39 years.

TABLE 5. Summary of Membership Transactions, 1982-1991

Transaction	Dec. 31, 1982	Dec. 31, 1983	Dec. 31, 1984	Dec. 31, 1985	Dec. 31, 1986	Dec. 31, 1987	Dec. 31, 1988	Dec. 31, 1989	Dec. 31, 1990	Dec. 31, 1991
Gains	1,527	2,242	2,169	2,037	2,213	1,880	1,838	2,042	1,907	1,847
New members	1,397	2,190	2,076	1,951	2,068	1,732	1,723	1,930	1,745	1,621
Reinstatements	130	52	93	86	145	148	115	112	162	226
Losses	642	588	661	714	757	867	976	1,002	1,197	1,486
Resignations	101	105	133	151	163	211	235	211	303	370
APA drops	266	226	312	249	281	336	328	412	457	526
District branch drops	38	34	61	77	101	136	87	164	232	174
Medical Student Mem- bers whose member- ship expired	0	0	0	0	0	0	0	0	0	152
Deaths	237	223	155	237	212	184	326	215	205	264
Net gain	885	1,654	1,508	1,323	1,456	1,013	862	1,040	710	361

Annual Meeting Workshop

The Scientific Program Committee accepted the Committee on Membership's proposal to conduct a workshop at the 1992 annual meeting in Washington, D.C. The focus of the workshop, an interactive meeting, will be on issues involving both membership recruitment and membership retention. District branch officers, staff, and chairpersons of membership-related committees are encouraged to attend and will be notified specifically of this workshop.

Dues Relief Criteria

A subcommittee of the Committee on Membership (Drs. Fuller and Coomaraswamy) will be redrafting criteria for use by the committee and the district branches in acting on requests for dues relief. Both the Constitutional and Assembly membership committees discussed at length the practice of some district branches of requiring financial statements from members who request dues relief. There were strong sentiments in both committees that this requirement poses confidentiality problems and that district branches should ask only for relevant information pertaining directly to the request. A letter will be sent by the Committee on Membership to all branches, highlighting this concern.

Committee on Young Psychiatrists

The Committee on Membership has been working with the Committee on Young Psychiatrists, which has requested longitudinal studies and a study of issues related to the retention of young psychiatrists (a "young psychiatrist" is under 40 years of age and/or has completed psychiatry residency training within the past 5 years). After meetings between representatives of both membership committees and staff, it appears that compromises have been reached which fulfill the needs of the Committee on Young Psychiatrists, taking into account current budgetary limitations. The Committee on Young Psychiatrists originally had asked that the Office of Membership undertake studies which could not be performed with current staff levels; the Committee on Young Psychiatrists is considering working with information that the Office of Membership can provide easily on a periodic basis.

Foreign Psychiatrists Who Receive Specialized Training in the United States or Canada

The Committee on Membership agreed that foreign-trained psychiatrists who come to the United States or Canada for a specified period of time to receive specialized training in psychiatry, who are not eligible for either Member-in-Training status or General Member status, shall be considered special applicants to be presented to the Committee on Membership for consideration as nonvoting, dues-exempt Corresponding Members, as they would be if they applied from their home countries. The local district branches would be encouraged to include these Corresponding Members in branch activities.

Ethnicity

The Committee on Membership has been discussing how race/ethnicity information is collected on the General Membership application form. The committee decided to return to a simplified race/ethnicity question that has single categories for Hispanic and Asian designations.

6-Year Limit for Members-in-Training

A Member-in-Training asked the Committee on Membership to consider changing the 6-year Constitutional time limit for Member-in-Training status. She expressed the concern that women are not always able to complete training within 6 years, especially if they have family obligations. The committee felt that the current system (including the process for granting waivers or Inactive status) allows flexibility and can meet demands of Members-in-Training whose training takes longer than 6 years.

International Membership

The Committee on Membership, at the request of the Joint Reference Committee (upon request by the Council on International Affairs), briefly discussed international membership. The committee would like to meet with the Director of APA's Office of International Affairs, Ms. Ellen Mercer, at its next meeting to explore increasing the international membership base and related issues.

Membership Termination for Members Eligible for Life Status

The Committee on Membership expressed great concern regarding the termination of membership for nonpayment of local dues of two Southern California Psychiatric Society members who had been members for 33 and 30 years, respectively. Both of these members would have become eligible for Life Member status on Jan. 1, 1992. The chairperson of the committee will write to the president of the district branch to express the sentiments of the committee and to ask the district branch to reconsider these membership actions. The Office of Membership earlier had requested that the district branch reconsider and waive the dues but to no avail.

ACTION ITEMS—GENERAL

Membership Directory

The committee reviewed a proposal from the Council on Research that the production of a membership directory be returned to the Committee on Membership and the Office of Membership. Given the complexities of producing a directory like the previous biographical directories, a number of options were reviewed: publish a smaller directory in-house; continue to use essentially the same approach but publish substantially less information on each member; continue to use the same approach and publish the same amount of information

on each member; collect and correlate a computer-based directory with sale of computer disks or use of a 900 telephone number; contract out the entire data collection, directory publication, and marketing effort.

After considerable discussion, the committee voted to accept the task of holding a feasibility meeting in early 1992 to explore issues surrounding responsibility for publishing a membership directory. The issues involved are many. The task may be complex, and a decision on the direction to be taken should be thoroughly considered in a session with adequate time and with adequate staff resources and background data.

The feasibility study group met in both February and March of 1992 to continue exploration of this question. The group included selected members of the Committee on Membership, the chairperson of the Committee on Biographical Directory and Research on Psychiatric Professional Activities, and selected staff. The group decided that a basic membership directory should be produced in 1994 (possibly to coincide with the Sesquicentennial annual meeting) and that the Committee on Membership and Office of Membership should undertake this project. The study group defined a basic list of items that could be included in such a directory but has not yet determined the final list of what information to collect. Staff is now working to prepare a timetable for this project and several possible budgets.

Military Psychiatrists

The Committee on Membership met with James R. Rundell, M.D., Major, U.S. Air Force, and President of the Society of American Military Psychiatrists. The two membership committees agreed to propose that a worldwide military branch of APA be created. It was noted that military psychiatrists, who number over 450, have already organized themselves into a society functioning in a manner similar to the district branches. The society has about 300 members. APA has approximately 100 military members.

It was felt strongly that military psychiatrists are a unique group because they are subject to frequent and sometimes involuntary relocations, hindering involvement in their geographic communities and hence those district branches. Lack of continued involvement in local district branches disenfranchises this group, makes participation in the governance structure difficult, and inhibits professional contact outside of the military, thereby preventing access to Fellowship. Their day-to-day ties and sense of community are with their military colleagues stationed all over the world and not restricted to the community where they happen to be stationed. The military psychiatrists feel strongly that their "community" consists of their military psychiatric colleagues. Their organization already meets on a regular basis. It maintains a mailing list and produces a periodic newsletter. Military psychiatrists also maintain regular contacts with one another through referrals and WATTS-line communications.

This matter has come before the committee in the past, without closure; however, for the first time the committee is convinced that, because of their establishment of their own organization, military psychiatrists are willing and able to assume responsibilities that are normally associated with the operations of a district branch, including addressing ethical matters, holding regular meetings, and maintaining membership records.

The proposal for a military branch would contain a provision allowing a military psychiatrist the option of belonging to the local district branch in lieu of the military branch. This is akin to a member's being allowed to belong to the district branch where she or he either practices or resides. The Assembly members for this branch would attend meetings of their closest Area councils, as is the case for our minority and Member-in-Training groups. It was the intent of the Committee on Membership that all of the officers of this branch would reside in the United States because of the costs of attending necessary meetings.

In November 1991 the Assembly voted to consider the special membership needs of worldwide active-duty military psychiatrists eligible for APA membership. Among the options to be explored are 1) recruitment for APA membership of the approximately 75% of active-duty military psychiatrists who are not members of APA, 2) facilitating application for advancement to Fellowship and inter-district-branch transfer of existing APA members, 3) enfranchisement in the Assem-

bly, 4) dues issues, and 5) possible creation of a worldwide armed forces district branch. The Assembly further voted to refer this entire matter to the Assembly's Committee on Planning for further evaluation and action recommendations by May 1992. In December the Board of Trustees endorsed the actions taken by the Assembly.

The Assembly's Committee on Planning considered this question when it met in February 1992. That committee plans to invite a member of the Committee on Psychiatric Services in the Military, a representative from the Society of American Military Psychiatrists, and people from the states with large military populations to its 1992 summer meeting.

Work Group on Membership Losses

Dr. Aron Wolf, chairperson of the Ad Hoc Work Group to Advise the Committee on Membership on Membership Losses, reported on the second meeting of the work group, held Nov. 7, 1991. Market research on APA membership and services, suggested by Mr. Rich Feeley (APA consultant), was discussed. The proposal calls for conducting focus groups and a survey as a means of obtaining accurate and meaningful information on member opinions regarding membership benefits (insurance, publications, etc.) and of learning more about factors governing the decision of members to join, or remain in, APA. Focus topics will include fiscal, branch, and publication issues in an attempt to compile comprehensive data in these areas. The estimated cost of such an undertaking is estimated to be around \$100,000; the understanding is that much of this expense would be borne by the APA Insurance Purchasing Group. The balance (estimated to be approximately \$30,000) would be drawn from APA and contributions from other entities (such as the American Psychiatric Press and the Corporation for the Advancement of Psychiatry) in exchange for inclusion of questions that relate to their interests. The data from these marketing studies should become available for possible action in the fall of 1992.

Staff received several proposals from companies experienced in this type of work. One proposal was selected, and the company accepted the contract for the project. Work is now underway on planning a series of focus groups around the country. Information collected from the focus groups will be used to conduct a more extensive survey of the membership on the same subjects. The results of the completed project will be reported to the Assembly and Board of Trustees in the fall of 1992.

Membership Eligibility

The Committee on Membership was asked to review the application for General Membership of a psychiatrist partially trained abroad. This psychiatrist completed residency in the United States and had been accepted for certification examination by the ABPN. The committee would like to recommend to the Board of Trustees that proof of acceptance for examination by the ABPN or the Royal College of Physicians and Surgeons (Canada) be accepted as a method of demonstrating eligibility for APA General Membership for psychiatrists trained outside the United States and Canada. The language to be proposed for inclusion in the "Operations Manual of the Board of Trustees" will be reviewed by the committee at its next meeting.

ACTION ITEMS—MEMBERSHIP PROCESSING

Accreditation by American Osteopathic Association

The Committee on Membership reviewed a request from the Iowa Psychiatric Society regarding eligibility for Member-in-Training (and subsequent General Member) status for an Iowa resident undergoing psychiatric training in a formerly ACGME-approved program now approved only by the American Osteopathic Association. The committee recommended that the resident not be considered eligible for membership unless he enters (and completes) an ACGME-approved training program.

Member-in-Training Advancement in Massachusetts

The committee reviewed requests from the Massachusetts Psychiatric Society regarding the eligibility for membership of two of its

members. The first, a Member-in-Training in an outpatient psychiatry fellowship, trained abroad and did not meet the criteria for advancement to General Membership in the opinion of the Committee on Membership. The second, an applicant for Member-in-Training status, was not deemed eligible for membership by the committee because his training program is not approved by the ACGME. The committee recommended that these membership applications be deferred.

Training Begun Abroad

The New Jersey Psychiatric Association requested that the committee review the application for General Membership of a psychiatrist whose psychiatric training began in Israel and was continued in the United States (the applicant had been accepted for the ABPN certification examination). The committee recommended, on the basis of documentation of U.S. training, that the psychiatrist be accepted for General Membership.

Retroactive Enrollment

A member requested that the Committee on Membership approve a change in his original enrollment date from 1971 to 1970. His application for Member-in-Training was submitted to the Northern California Psychiatric Society on Sept. 20, 1969, and forwarded to APA on March 29, 1971. He was accepted as a Member-in-Training on May 1, 1971. The committee could not find sufficient evidence of any administrative error to justify granting the request and recommended denial.

Fellowship Nominations

The committee reviewed 223 nominations for Fellowship; 182 (81.6%) were recommended for approval by the Board of Trustees (see table 4). The approval rates in 1990 and 1989 were 75.4% and 85.9%, respectively.

Nominations for Honorary Fellowship and Distinguished Fellowship

In accordance with the "Operations Manual of the Board of Trustees," the Committee on Membership acts on nominations by voting members of the Association for Honorary Fellowship and Distinguished Fellowship and forwards its recommendations to the Board of Trustees.

A letter nominating Jean Endicott, Ph.D., for Honorary Fellowship was received from a Fellow of APA. The committee reviewed two additional letters of support and recommended approval of Dr. Endicott for Honorary Fellowship.

A letter nominating Patricia van Ameringen Kind, Ph.D., for Honorary Fellowship was received. The committee reviewed three additional letters of support and recommended approval of Dr. van Ameringen Kind for Honorary Fellowship.

A letter nominating Rachel Gittelman Klein, Ph.D., for Honorary Fellowship was received from a Fellow of APA. The committee reviewed four additional letters of support and recommended approval of Dr. Klein for Honorary Fellowship.

The committee reviewed a request from the Texas Society of Psy-

chiatric Physicians asking for permission to elevate an Associate Member, Leo E. Hollister, M.D., to General Membership even though Dr. Hollister never completed formal psychiatry training and therefore is not eligible for General Member status. The committee concluded, on the basis of Dr. Hollister's very significant and sustained contributions to the field and the strong supporting letters, that Dr. Hollister should be nominated for elevation to Distinguished Fellow. While the committee recognized that the customary procedure for bringing such a nomination to the Board was not followed, it strongly believed that Dr. Hollister met the necessary criteria and recommended approval of Dr. Hollister for Distinguished Fellowship.

Corresponding Members/Fellows

The committee reviewed applications for membership/advancement and recommended that 31 applications for Corresponding Membership and six nominations for new Corresponding Fellows be accepted and that decision on one nomination for advancement from Corresponding Member to Corresponding Fellow be deferred.

Membership Termination for APA Dues Arrears

In compliance with chapter 8, section 7, of the Constitution and Bylaws, the committee recommended that the members whose dues were in arrears for 1990 be dropped from APA membership.

Resignations

Under standing authorization of the Board of Trustees, the Medical Director regretfully accepted the resignations of 370 members during 1991.

Dropping of Members Dropped by District Branches

Chapter 8 of the Bylaws states, "Resignation or loss of membership in the Association or the member's district branch for any reason shall entail loss of membership in both." During 1991, 174 members resigned from or were dropped by their district branches. They were advised that loss of branch membership would involve loss of APA membership. The committee recommended that the Board of Trustees authorize the dropping from APA membership of members who had resigned from or had been dropped by their district branches and, further, that the Board of Trustees authorize administrative reinstatement of those who returned to good standing in their district branches and were also in good standing in APA.

Dues Relief/Inactive Status

The committee reviewed 391 requests for dues relief and/or transfer to Inactive status and recommended approval of 319 and deferral or denial of 72 (see table 4).

Expiration of Medical Student Membership

Numerous Medical Student Members have graduated from medical school, and therefore they have been sent letters notifying them that their Medical Student Membership has expired and, if appropriate, they should advance to Member-in-Training status.

Report of the Committee of Tellers

John Zinner, M.D., Chairperson

The Committee of Tellers met on March 20, 1992, at APA headquarters to certify the results of the 1992 election. Ballots were mailed on Feb. 5, 1992, to 34,715 eligible voting members; from that number 156 undeliverable ballots were deducted. The adjusted number of eligible voting members was 34,559, and 14,260 ballots were returned and included in the final tally (41.3% of the eligible voting members).

The Committee of Tellers acted on uncertain votes that had been held for their decisions. The committee also confirmed that all candidates had verified the accuracy of their biographical statements and had submitted the required statements of compliance with election guidelines.

The Committee of Tellers certified that the following individuals were elected to office and so reported to the Board of Trustees—President-Elect: John S. McIntyre, M.D. (59.6% of the votes cast); Vice-President: Lewis L. Judd, M.D. (57.7%); Treasurer: Mary Jane England, M.D. (69.0%); Trustee-at-Large: Benjamin Liptzin, M.D. (52.0%); Member-in-Training Trustee-Elect: Marian I. Butterfield, M.D. (53.9%); Area III Trustee: Abram M. Hostetter, M.D. (59.7%); Area VI Trustee: Daniel B. Borenstein, M.D. (57.1%).

To have a valid election on changes to the Constitution and Bylaws, 33⅓% of the eligible voting members must cast votes. Abstain and invalid votes are considered to be votes cast and count toward determining whether 33⅓% has been reached. Abstain and invalid votes do not count in determining whether a change passes or fails. Once 33⅓% has been reached, a majority must approve amend-

ments to the Bylaws. The results of the vote on the amendments are as follows.

Amendment 1, chapters 1.13 and 8.6. Votes were cast by 39.3% of the eligible voters. The amendment passed; 66.6% of the votes were in favor. The change removes the dues exemption of members who achieve Life status according to the "rule of 95" in 1993 and thereafter, and it requires them to pay two-thirds dues during the first 5 years after they achieve Life status and one-third dues during the second 5 years. The dues exemption of members who achieved Life status before 1993 continues.

Amendment 2, chapter 6.5. Votes were cast by 39.3% of the eligible voters. The amendment passed; 66.9% of the votes were in favor. The change expands the Nominating Committee to include a representative of a minority/underrepresented group selected in a manner similar to how Area representatives to the Nominating Committee are selected.

Amendment 3, chapter 9.1. Votes were cast by 39.2% of the eligible voters. The amendment passed; 68.3% of the votes were in favor. The change increases the number of signatures required for nomination by petition from 200 to 400 for national office and from 50 to 100 for Area Trustees.

On the recommendation of the Committee of Tellers, the Board of Trustees accepted the results of the 1992 election. The Board also approved a recommendation of the committee to dispose of the ballots from the 1992 election after the 1992 annual meeting.

THE AMERICAN JOURNAL OF PSYCHIATRY

Special Articles

Psychosocial Rehabilitation and Psychiatry in the Care of Long-Term Patients

Leona L. Bachrach, Ph.D.

The relationship between psychosocial rehabilitation and psychiatry in the care of long-term mental patients is one that may often be characterized, at best, as an uneasy alliance. The author summarizes the basic concepts that define the discipline of psychosocial rehabilitation and discusses how those concepts have at times been distorted in actual practice. The article concludes with an analysis of the two disciplines' common ground in caring for long-term patients and a commentary on the benefits that each may offer the other. Together psychiatry and psychosocial rehabilitation hold the key to improved circumstances for realizing the promise of deinstitutionalization, which seems largely to have eluded us for the past several decades.

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During the past several decades psychosocial rehabilitation has achieved prominence as a major service modality in the care of individuals with long-term mental illnesses. Meyerson and Solomon wrote that the field "has received increasing acceptance as a viable treatment approach for those who have severe mental disabilities" (1, p. 1), and Anthony et al. predicted that during the 1990s psychosocial rehabilitation "will assume its rightful place" (2, p. 1).

Yet the relationship between psychosocial rehabilitation and psychiatry in the care of long-term patients is one that may often be characterized, at best, as an uneasy alliance. Although there are certainly service systems and individual agencies in which the two disciplines' offerings are blended to the benefit of the patients whom they serve (3, 4), there are also numerous instances of mutual mistrust. For example, Ryan et al.

wrote that "traditional forms of psychiatric treatment for persons with schizophrenia have led to very poor outcomes" (5, p. 67) and that psychosocial rehabilitation "may well be the preferred way of treating the psychological condition of the person with schizophrenia" (5, p. 83).

To some extent, such statements probably reflect heightened turf concerns (6). An unfortunate result of diminishing resources for the treatment of long-term mental patients may be increased suspicion of the motives of competing disciplines, particularly when interdisciplinary conflict is already entrenched (7, 8). That differences in ideology may be perceived, however inaccurately, as incapable of resolution probably further contributes to the schism. But whatever its source, mistrust between the two disciplines, when it occurs, violates the very basis of multidisciplinary care as envisioned by President John F. Kennedy (9) in the early days of community mental health.

The polarization of psychiatric treatment and psychosocial rehabilitation, in its most extreme form, may be characterized as consisting of two irreconcilable myths. One of these has arisen among certain nonpsychiatric clinicians who hold that rehabilitation is the only kind of modality that persons with long-term men-

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tal illnesses require and that all other interventions are superfluous, if not harmful. This myth essentially encourages the minimization or even total elimination of psychiatric care for long-term mental patients, and the dangers inherent in it are readily apparent to those familiar with the debilitating effects of severe mental illness. However, a second, equally dangerous myth has arisen within psychiatry, and it holds that rehabilitation philosophy is intrinsically antimedical in its orientation and so must be radically revised, if not eliminated.

In this article I seek to dispel these myths by demonstrating that there is actually a great deal of concordance between the philosophies of psychiatry and psychosocial rehabilitation as they relate to the care of long-term mental patients. I shall argue that the two disciplines need not—in fact, should not—be mutually exclusive. Toward that end, I shall begin with a summary of the basic concepts that define the discipline of psychosocial rehabilitation as it is described in the literature and proceed to a discussion of how those concepts have at times been distorted in actual practice. I shall conclude with an analysis of the two disciplines' common ground in caring for long-term patients and a commentary on the benefits that each may offer the other.

It is probably appropriate for me to state my bias at the outset. I have long been a proponent and student of psychosocial rehabilitation. In fact, my connection with the field of rehabilitation dates back to the time of my first-professional job in the 1950s, when, as a graduate student, I was hired by a facility known today as the Rusk Institute to assist in the piloting of a psychosocial adjustment questionnaire for physically handicapped persons.

Although the terms "psychosocial rehabilitation" and "psychiatric rehabilitation" appear today to be used interchangeably—any distinctions that might once have existed between them have become blurred in the current literature—this article will use the former term and reserve the adjective "psychiatric" to refer more specifically to concepts and interventions that are exclusively associated with the practice of psychiatry.

DEFINING PSYCHOSOCIAL REHABILITATION

The field of psychosocial rehabilitation consists of several different approaches to the care of individuals who suffer from long-term mental illnesses. There are, for example, intradisciplinary differences over what specific training should be required for the credentialing of rehabilitation practitioners, as there are in the degree to which specific modalities, such as behavior modification and psychoeducation, are used.

It is not my intent to comment on the relative merits of these several "models" of psychosocial rehabilitation. Rather, my aim in this article is to focus on their common ground in order to provide readers with a basic, "least common denominator" understanding of the field. This task is, however, complicated by the fact

that, to my knowledge, there is no commonly endorsed definition of psychosocial rehabilitation in the literature (10–12). It is probably not far-fetched to suggest that at least some of the friction which sometimes surfaces between this discipline and psychiatry derives from the fact that, in the absence of a precise definition, psychiatrists' notions about psychosocial rehabilitation are often vague and at times inaccurate.

However, unlike some other occasions in mental health where a single imprecise concept conceals differences that appear to be virtually irreconcilable (13), the several approaches that define themselves as psychosocial rehabilitation appear to share a core of common concepts and values, at least insofar as these are expressed in the literature. This shared philosophy is captured in the writings of Cubelli and Havens (14) and Liberman (15), whose definitions of the field may be paraphrased and summarized as follows: psychosocial rehabilitation is a therapeutic approach to the care of mentally ill individuals that encourages each patient to develop his or her fullest capacities through learning procedures and environmental supports.

ESSENTIALS OF PSYCHOSOCIAL REHABILITATION

As revealed by the field's literature, the philosophy underlying the practice of psychosocial rehabilitation consists of a minimum of eight fundamental and inter-related concepts. Perhaps the most basic of these is the discipline's central goal of enabling an individual who suffers from long-term mental illness to develop to the fullest extent of his or her capacities (6). The word "individual" must be heavily underscored, for psychosocial rehabilitation strongly rejects predetermined, stereotyped, and nonindividual notions of patient care and, first and foremost, emphasizes the need for individually tailored interventions. To express this concept somewhat differently, psychosocial rehabilitation typically rejects questions about what might constitute an appropriate treatment for an entire population of long-term mental patients and focuses instead on what would constitute appropriate care for one specific patient.

Second, in conjunction with individually oriented interventions, psychosocial rehabilitation stresses the importance of environmental factors in the care of people with long-term mental illnesses (16). Because "the essential starting point for a proper understanding of rehabilitation is that it is concerned with the individual person in the context of the environment" (12, p. 3), psychosocial rehabilitation requires either that the patient's capacities be adapted to environmental realities or that the environment be changed to suit the capacities of the patient (17). This focus on environmental concerns also characterizes the practice of clinically oriented case management, which, in addition to providing direct patient care, also encompasses the creation, modification, and adaptation of social and physical environments in order to meet the needs of individuals with long-term mental illnesses (18).

Third, psychosocial rehabilitation is oriented toward the exploitation of patients' strengths (19). Its primary concern, according to Anthony et al., is with "improving the competencies" of people who have long-term mental illnesses (2, p. 64). In fact, this feature of psychosocial rehabilitation is reflected in the position long taken by Lamb, a psychiatrist, who has suggested that clinicians "must work with the well part of the ego" and has contended that "regardless of the extent of psychopathology in evidence, there is always an intact portion of the ego to which treatment and rehabilitation efforts can be directed" (20, p. 7).

Psychosocial rehabilitation is thus eminently positive in its philosophy (12), and this leads directly to a fourth, closely related essential feature of the discipline: the aim of restoring hope to individuals who, because of their psychiatric illnesses, have suffered major setbacks in functional capacity and self-esteem. Anthony et al. have written that "hope is an essential ingredient of psychiatric rehabilitation" (2, p. 67) and have described the focus on hope in terms of the discipline's "future-orientation." This emphasis, as intangible as it is positive, emerges as a distinguishing feature of psychosocial rehabilitation, particularly when it is compared with some of the more traditional psychiatric approaches to the care of patients with long-term mental illnesses (15). Although I know of no formal content analyses to cite in this regard, I would submit that discussions of hope are standard fare in the psychosocial rehabilitation literature but only rarely appear in psychiatric writings on service planning.

The centrality of hope as a concept in psychosocial rehabilitation has been discussed at length by Deegan (21), a clinical psychologist who at one time in her life was hospitalized for schizophrenia: in an address given at a conference in 1988, she said, "For those of us who have been diagnosed with mental illness hope is not just a nice sounding euphemism. It is a matter of life and death." Deegan has revealed that, early in her illness, a loss of hope led her to inactivity and intense depression: "When one lives without hope (when one has given up), the willingness to 'do' is paralyzed as well" (21, p. 13).

A fifth essential concept in psychosocial rehabilitation is its optimism about the vocational potential of mentally ill individuals (2, 22). Van Weeghel and Zeelen (23) in The Netherlands have summarized five advantages of pursuing vocational goals in rehabilitation. First, and most obviously, work provides an income that permits mentally ill people autonomy in gaining goods and services; second, work provides these individuals with the kind of time and space structure that Lamb (20) has described as being critical in the treatment of chronic mental illness; third, work has the potential for broadening the social contacts of mentally ill people; fourth, work provides the person with a readily recognizable societal role; and, fifth, work forces individuals to be active and involved. Similarly, the British rehabilitation psychologist Shepherd has written that work gives the individual patient "a sense of personal achievement and mastery" and that "no other sin-

gle activity is so rich and complex in its psychological, social and material significance" (24, p. 124).

Work is, of course, central to the well-known Fountain House approach to psychosocial rehabilitation, as is demonstrated in the following statement: "Work, especially the opportunity to aspire to and achieve gainful employment, is a deeply generative and reintegrative force in the life of every human being" and, as such, it "must underlie, pervade, and inform" all of the activities surrounding rehabilitation (19, p. 67).

It must be noted, however, that the vocational emphasis in psychosocial rehabilitation is not limited to the pursuit of full-time or competitive employment. For some long-term mentally ill persons the notion of work must be more broadly defined (25-27). Jones, who organized the excellent, but now superseded, Boardwalk program in Denver, has expressed the need for such flexibility in her statement that work opportunities for long-term patients "should address a variety of skills and interests and a variety of physical demands . . . in part because different people have different talents . . . [and in part] because the effects of the illness vary considerably" (28, p. 53). Similarly, van Weeghel and Zeelen have suggested that "vocational rehabilitation does not refer to the regular job market as a single final objective for everybody, but is above all a process with variable elements and differing results" (23, p. 4).

In this connection, supported employment opportunities, which use personal job coaches to provide support to workers and to ensure job backup to employers (29), are important aspects of many psychosocial rehabilitation programs.

Sixth, although psychosocial rehabilitation efforts generally place considerable emphasis on vocational pursuits, this represents only one area of their involvement (30). The field generally views its mission as reaching beyond work activities to encompass a full array of social and recreational life concerns of mentally ill people. Thus, it is not uncommon for psychosocial rehabilitation agencies to sponsor social clubs and to offer resocialization programs and training in social skills. They also frequently provide case management services, as well as various kinds of residential programs, educational activities, community support interventions, consumer-run drop-in centers and businesses, and even family education and support programs (11, 19, 24, 31-35). In short, psychosocial rehabilitation is at heart oriented toward the comprehensive care of individuals with long-term mental illnesses.

Seventh, psychosocial rehabilitation requires that patients be actively involved in their own care and, indeed, in the very design of their own rehabilitation protocols. Thus, in the words of Anthony et al. (10, p. 74), the patient's own "values, experiences, feelings, ideas, and goals" shape the direction of treatment planning during all phases of a rehabilitation intervention. In turn, this requires that the patient be completely informed about the nature of his or her illness, its symptoms, its course, and its possible consequences.

Such an emphasis on patient involvement stands in

direct contrast to interventions and treatments that do "to" or "for" patients, instead of giving them the scope to do "to" or "for" themselves. Peterson, a former patient who has written about his experiences as a member of the renowned Fountain House program in New York City, has expressed this distinction clearly and forcibly in a simple but revealing statement: "For me rehabilitation is not having something done to me" (36, p. 49). Some rehabilitation programs actually go so far with the concept of patient involvement that they are, in effect, consumer-run—and sometimes even consumer-directed—efforts (37).

Eighth, psychosocial rehabilitation is not a one-time-only kind of intervention. It is an ongoing process that must continue over time, and it is conducted in the various settings in which patients find themselves. Hence, rehabilitation programs, although viewed by many persons as having an essential community focus, may also be provided in hospital-based settings; the "where" of a rehabilitation effort is less important than what occurs in a given program and how long that program will be available to the patient (2, 12). Psychosocial rehabilitation is, in short, firmly wedded to the concept of continuity of care (38), a focus that is buttressed by several theoretical underpinnings.

First, there is a strong emphasis on the fact that mentally ill persons exhibit different functional deficits in different social environments. It follows that changes in the external circumstances of these individuals will require ongoing modifications in their basic rehabilitation protocols and that interventions will have to be persistent and flexible (12).

In addition, there is evidence that mentally ill persons generally find it difficult to transfer learned skills and behaviors to new situations (12). Psychosocial rehabilitation must thus "operate on the principle that generalization does not just occur; it must be planned" (10, p. 74).

Moreover, the vulnerabilities of people with long-term mental illnesses are not time limited (unpublished 1990 paper of J.W. Louwrens). To the contrary, they are often lifelong and so require continuing intervention. (The implications of enduring disability for the care of long-term mental patients will be examined more fully in the discussion that follows.)

These eight basic elements of psychosocial rehabilitation, when considered together, suggest that the discipline is, both in theory and practice, prepared to consider and respond to the interaction of a multiplicity of biological, psychological, and sociological factors as they influence the life of a mentally ill individual (31). Thus, psychosocial rehabilitation may be understood to favor a distinctly biopsychosocial approach (39) to the care of people with long-term mental illnesses.

THEORY VERSUS PRACTICE

It is, however, important to note that these theoretical guidelines are not always observed in practice. There is

sometimes a gap between the real and the ideal, just as there may be in the practice of psychiatry with long-term mental patients (40). My own observations during site visits to numerous psychosocial rehabilitation programs throughout the United States have led me to conclude that a few of them are so extremely antimicrobial and antipsychiatric in their outlook that they are, in my judgment, quite dangerous for the patients enrolled in them. These programs strongly resist the use of medications for severely mentally ill individuals and tend to regard the involvement of medically trained personnel as something to be avoided at all costs. In fact, sometimes these efforts are not limited to antimicrobial sentiments; they are also more generally antiprofessional, in that they seem to regard clinical training as something that takes the humanity out of patient care (7).

On a more positive note, it appears to me that such blatantly antiprofessional programs have been decreasing in number. Apparently, an acknowledgment that illness—real illness—underlies psychiatric disability (41) is growing, perhaps in part as the result of the increasing visibility of untreated mentally ill people who now live on the streets. However, some of the biased programs have survived and have unfortunately given psychosocial rehabilitation a bad name. That is why it is extremely important for the field to define precisely what psychosocial rehabilitation is—and also what it is not.

Somewhat less abusive than these blatant denials of illness, but still in my judgment far too antitherapeutic for comfort, is the existence of unrealistic expectations of long-term mental patients in some psychosocial rehabilitation efforts. I have observed a number of instances in which personnel expect mentally ill individuals to accomplish tasks that would be unrealistic for even less disabled persons. I refer specifically to the regimentation that creeps into some programs and virtually forces mentally ill people always to do something, to complete something, to go somewhere, or to be somewhere. Of course, rehabilitation is by its very nature task oriented; that is a given. But it seems obvious that there must be a limit to the pressure that is placed on patients to perform.

Another antitherapeutic practice exists in the tendency of some psychosocial rehabilitation efforts to close their gates—and, more importantly, to close their consciousness—to the most severely disabled mentally ill individuals. As a matter of fact, it is not the gatekeeping *per se* that is troublesome; few if any programs fail to exercise some control, however minimal, over admissions. What is of concern, however, is the existence of programs that purport to keep no gates but then proceed to admit only individuals who appear to fit in with their special offerings—a practice that sometimes leaves patients who do not fit with no alternatives for treatment.

Such gatekeeping practices are closely related to still another difficulty: the tendency of some psychosocial rehabilitation programs, despite lip service to flexibility, to place such heavy emphasis on the vocational aspects of rehabilitation that other important concerns

become minimized. Speaking of rehabilitation for physically disabled persons, Litman (42) cautioned that, when programs are too focused on vocational objectives, they may become "dominated by a utilitarian goal of employability." This systematically discriminates against persons who are unemployable.

Litman's concern is as valid for psychiatric patients as it is for physical medicine patients. For one thing, external economic circumstances, as well as the degree of competition within the labor force, may severely curtail employment opportunities for mentally ill people (30; unpublished 1990 paper of J. van Weeghel). Additionally, the stresses that these individuals sometimes suffer when their efforts to find work are unsuccessful may be quite harmful, particularly when competitive employment is held up as the ultimate goal for every person.

I mention these issues not because they are intrinsic to the practice of psychosocial rehabilitation or even necessarily illustrative of mainstream thought in the field but, rather, because, when such negative practices occur, they serve mentally ill individuals poorly. Moreover, these negative practices—these departures from the ideal—are completely antithetical to the fundamental philosophy of psychosocial rehabilitation as it is portrayed in the extensive literature of that field. In fact, from the point of view of that literature, it may well be an error to define the efforts that foster such practices as rehabilitation programs. Yet, in the absence of a standardized definition of what the field encompasses, there is nothing to stop them from identifying themselves in this way.

On a more positive note, even a cursory review of the literature suggests that these problems are increasingly being acknowledged within the field of psychosocial rehabilitation. This gives us hope for their amelioration. Lamb (20) has been particularly forthright in identifying these kinds of issues and in cautioning against what he has termed the "overselling" of rehabilitation. Fortunately for all concerned, Lamb's writings continue to have considerable impact on service planning for long-term patients.

CONCEPTS IN PSYCHIATRIC CARE

One of the most harmful effects of the negative practices I have described is that they reinforce an impression that the disciplines of psychosocial rehabilitation and psychiatry lack a common meeting ground. Is such a conclusion valid? To answer this question I have selected two major conceptual developments that influence the psychiatric treatment of long-term mental patients today (43), and I shall use these as yardsticks for establishing the degree of fit between the two disciplines. I shall first comment on the psychiatric concept of individualized treatment planning for long-term mental patients and then examine a psychiatric approach to the understanding of disability among the members of this patient population.

My choice of the psychiatric concept of individualized treatment planning may perhaps appear gratuitous. Does it not go without saying that psychiatric care will be administered with a focus on the individual patient? Unfortunately, this has not always been the case, as is apparent from the frequency with which "dumping" of long-term mental patients has occurred. These patients have frequently been placed in institutions and provided, at best, with only stereotyped programming. What is more, they have often fared no better in their community placements (44). Indeed, the fact that the mental patients who need the most comprehensive and sophisticated care have historically been given the least individualized treatments has become a source of great concern to many psychiatrists (40). (I might add that, as an involved nonpsychiatrist, I believe the future credibility of psychiatry will rest largely on its ability to organize individually tailored treatments for long-term patients as effectively as it has in the past for patients who are less severely disabled.)

It is encouraging to note, however, that in recent years the psychiatric literature has shown increasing concern with the need to accord individualized attention to long-term mental patients (38, 45). The concept of individualized treatment planning is now widely endorsed and forms a potential bridge between the practice of psychiatry and that of psychosocial rehabilitation. As noted earlier, the basic orientation of rehabilitation is toward the individual patient—toward realistically assessing that person's strengths and disabilities and working from there to maximize his or her potential. Thus, it seems unnecessary to belabor the point: the fit between psychiatry and psychosocial rehabilitation respecting this particular concept leaves little if any room for theoretical dissonance.

Indeed, the fact that both disciplines speak with a single voice on this issue is most encouraging. Whether it gets its impetus from psychiatry or psychosocial rehabilitation, the acknowledgment that programmatic interventions must stress the needs of a mentally ill *person*, and not the needs of a mentally ill *population*, is a major step forward in service planning. It is even possible that this is the most important advance in service planning for long-term patients over the past several decades (45), and the concordance between the two disciplines in this regard is readily apparent.

The relationship between the psychiatric concept of disability and the practice of psychosocial rehabilitation is somewhat more complex, although it too suggests considerable congruence between the two disciplines. Increasingly today, disability is viewed as having multiple sources that subsume, but extend beyond, the direct effects of psychopathology. There have been several formulations of this position in the psychiatric literature, including the focus on impairment, disability, and handicap that is largely associated with the rehabilitation approach of Liberman et al. (15, 16). As a sociologist, however, I am drawn to the particular constructs and terminology used by two British authorities; Wing and Morris (46).

Wing and Morris have described three essential varieties of disability that typically affect severely ill long-term mental patients. The primary disabilities are those associated with the illness per se; they consist of dysfunctional behaviors or characteristics that may otherwise be described as symptoms of illness. For example, people diagnosed with chronic schizophrenia might exhibit such primary disabilities as lethargy, odd and unacceptable behavior, a lack of awareness of their handicaps, and disturbances in their social relationships. It is typically the appearance of these symptoms of illness that leads to diagnosis and, for many individuals although not all, to treatment in the system of care.

Building on the primary disabilities are secondary disabilities that come not from the illness per se but from the *experience* of illness. Wing and Morris have referred to these as "adverse personal reactions," and their essence was eloquently captured in an anonymous patient-authored article that appeared in the *American Journal of Psychiatry* several years ago: "Even if medication can free the schizophrenic patient from some of his torment, the scars of emotional confusion remain, felt perhaps more deeply by a greater sensitivity and vulnerability" (47).

Wing and Morris (46) have suggested that secondary disabilities may present as much of a problem for successful engagement and treatment of the long-term patient as do the primary symptoms of the illness itself. In fact, a critical point to keep in mind regarding secondary disabilities is that they are often difficult to overcome. In Shepherd's words, "a major psychiatric episode is a frightening and disturbing experience and its effects may persist long after the primary symptoms have disappeared" (24, p. 5).

Finally, there is a class of tertiary disabilities that Wing and Morris (46) call "social disablements." These come not from the illness per se, nor are they personal responses to illness. Rather, they are external to the patient and come from societal reactions to mental illness. Accordingly, the tertiary disabilities include such circumstances as diminished social networks, stigma, poverty, unemployment, and the general absence of a place in society.

A most succinct and moving description of tertiary disabilities was provided at a meeting in 1987 by a former mental patient, Esso Leete:

Sadly, in addition to handicaps imposed by our illnesses, the mentally disabled must constantly deal with barriers erected by society as well. Of these, there is none more devastating, discrediting and disabling to an individual recovering from mental illness than stigma. We are denied jobs, unwanted in our communities. We are seen as unattractive, lazy, stupid, unpredictable, and dangerous.

Inevitably, these societal responses spill over into the mental health service system and are manifested in program offerings for long-term patients that are frequently irrelevant and sometimes downright discriminatory and preclusive.

Lewis, an internist, described the biopsychosocial perspective as one that "frees us from biologically overdetermined and restrictive criteria and from vague definitions of disease" (48, p. 262). It is clear that such a concept is entirely consistent with the psychiatric formulation of disability described here—an approach in which biological, psychological, and sociological elements in interaction are understood to give rise to the problems experienced by long-term mental patients. Moreover, it seems obvious that such a concept of disability must also be entirely compatible with the philosophy of psychosocial rehabilitation, which is equally biopsychosocial. Both suggest that clinical interventions which can affect the lives of long-term mentally ill people in a positive and lasting way depend on the clinician's ability to respond simultaneously to all their sources of disability, not just their illnesses (16, 49).

TOWARD A COMMON FOCUS

Given this commonality in outlook, how may the two disciplines actually share in the clinical care of long-term mental patients? At the first level of disability—the level of the primary symptoms—programs that make the most effective use of pharmacotherapies are needed, for it is the competent and judicious prescription and monitoring of drugs that may start the reversal of primary symptoms and thus allow intervention at the other levels. Obviously, the medically trained psychiatrist has a basic role to play with respect to primary disabilities.

The psychiatrist also has an obvious and essential role with reference to the secondary disabilities by helping patients to understand, accept, and come to terms with their illnesses. In fact, psychiatry and rehabilitation can, and should, work together in this regard. They must make available to each patient a variety of interventions that will help him or her to respond more realistically to the fact of illness. This includes providing individual and group psychotherapy, counseling, psychoeducation, and, in the most basic way, a full array of rehabilitative interventions that relate to skills training, behavioral change, and environmental adaptation.

Areas of overlap between the two disciplines are also evident with respect to the tertiary disabilities. It is essential that agencies providing services to long-term mental patients seek to improve overall quality of care, enhance patients' social networks, minimize the negative effects of gatekeeping, and attempt to reduce stigma within the mental health professions and society at large. Rehabilitation, with its concept of engineering environmental change, effectively legitimizes the professional person's role in these kinds of efforts. Rehabilitators, psychiatrists, and everyone else involved in the care of long-term mentally ill individuals must be prepared to pressure the service system, from within and without, to alter its practices and become responsive to the social disablements of these individuals.

The Dutch psychiatrist F.M.J. Woonings, in an un-

published 1990 paper, defined psychosocial rehabilitation as "a process in which skills are being learned to cope with permanent disability." At first glance, non-psychiatrists might regard such a definition—one that is proffered by a psychiatrist and stresses the permanence of psychiatric disability—as unduly pessimistic. However, if considered in the context of Wing and Morris's concept of disability, this definition is entirely realistic. Since disability is not limited to circumstances that arise directly from the illness but also includes psychological and sociological elements, and since the latter may persist independently over time, the notion of permanent disability is entirely credible. What is more, it is absolutely consistent with rehabilitation's emphasis on continuity of care.

UNDERSTANDING THE CONFLICT

The foregoing discussion suggests substantial areas of compatibility between psychiatric and psychosocial approaches to the care of long-term mental patients. It is important to note that there exist a number of clinical settings in which that compatibility is put into practice and the two disciplines work together cooperatively and successfully. Some, like Liberman's programs (15), actually foster a blurring of the boundaries between the disciplines. The fact that instances of dissonance are often sounded loudly does not mean that they necessarily dominate in the relationship between the two fields.

But some dissonance does exist, and as noted previously, a portion is probably attributable to turf concerns that have become exacerbated by diminishing resources. The fact that it is difficult to know precisely what a psychosocial rehabilitation program is probably contributes to the dissonance as well: as we have seen, some programs that do not honor the philosophy of the discipline bear that name.

However, there is still another factor that may explain some of the interdisciplinary conflict. This is the fact that the comprehensive role of each discipline is inadequately understood, or perhaps not accepted, by the other. For example, proponents of psychiatric rehabilitation sometimes, and inaccurately, see psychiatry as following rigid "medical model" practices in the care of long-term mental patients; they overlook the fact that the biopsychosocial approach is but one of several medical models and is particularly supported by psychiatrists who work with this patient population.

Additionally, it is likely that a certain amount of conflict is related to the fact that psychosocial rehabilitation has been viewed primarily as tertiary prevention (16, 50, 51)—as part of a class of interventions that follow active treatment. It is not surprising that rehabilitation practitioners have become somewhat sensitive to this characterization of their work, a view that they feel, perhaps accurately, has been fostered by psychiatric clinicians and that minimizes their contribution during the active phases of a patient's illness.

Gittelman (52) has, however, proposed an alternative

view, one that establishes psychosocial rehabilitation as part of secondary prevention—as part of treatment instead of something that follows treatment. This notion, which is also reflected in the writings of Fine (6), a prominent occupational therapist, is almost certainly more in line with psychosocial rehabilitation's existential view of its mission and is worthy of serious consideration by psychiatrists.

In many ways, however, the controversy over boundaries is basically a meaningless one, a fact that Black recognized and cautioned against in 1978: "It matters little whether one considers rehabilitation as part of a total treatment or mental health approach . . . or whether one thinks of rehabilitation as the totality of the endeavor of which the medical and psychiatric treatment is a part. The fact is that there must be a joining of resources" (32, pp. 308–309).

REHABILITATION'S INTEGRATIVE FUNCTION

Many rehabilitation practitioners will readily acknowledge that the field of psychosocial rehabilitation depends on psychiatry in a number of ways. They understand, for example, that unless the primary symptoms described by Wing and Morris are under control, rehabilitative interventions are likely to have little success. They also acknowledge that in the case of illnesses with episodic exacerbations, it is essential to have medically trained personnel who are able to sort out the sources of patient dysfunction. Many also accept the critical importance of providing psychiatric therapy, individual and group, to long-term mental patients even as they are enrolled in psychosocial rehabilitation programs.

But what is the trade-off for psychiatry in allying itself with psychosocial rehabilitation? I would submit that, for psychiatry, there is valuable support to be found in the philosophy, goals, and practice of psychosocial rehabilitation. Psychosocial rehabilitation is, in essence, an integrative discipline in several different senses, all of them important for the practice of psychiatry.

First, psychosocial rehabilitation is integrative for patients in a psychological sense, in that it fosters wholeness in the individual. When it is pursued realistically and in a manner consistent with its philosophical foundation, psychosocial rehabilitation enables patients to develop a sense of hope and purpose that supplements—and may even enhance—more traditional treatment approaches. In this sense, psychosocial rehabilitation supports the goals that psychiatry holds for patients: to "live, love, and work meaningfully and productively in the world" (3). What is more, in the words of Gittelman and Freedman (53), if psychiatrists fail to support rehabilitative interventions, they will find themselves "treating only half the illness."

Second, psychosocial rehabilitation is also integrative for patients in the sense that it assists them in finding their place in the community. With its environ-

mental focus, psychosocial rehabilitation provides these individuals with the learning and skills that are necessary for societal integration. And with its emphasis on continuity of care, it helps ensure that those skills are constantly updated. This is entirely consistent with psychiatry's aim of enabling mentally ill individuals to function optimally in community-based settings. Needless to say, such societal integration cannot be complete for all patients, for we are not at present able to restore all mentally ill persons to full societal functioning. But even for patients whose integration will be marginal, rehabilitation represents a starting point. At the very least, it can provide positive experiences and hope for many people who suffer from long-term mental illnesses.

Third, from the point of view of the psychiatrist who seeks to reinforce his or her connection with other medical specialties, having a rehabilitative focus may serve still another integrative function. Anthony et al. (2) have shown that there is a close connection between the essentials of psychosocial rehabilitation and those of rehabilitation for physically disabled individuals, and Deegan wrote, "From the perspective of the rehabilitation approach, it is no longer necessary to isolate the psychiatrically disabled as totally different from other groups of persons with disabilities" (21, p. 11). Thus, psychosocial rehabilitation offers a tangible point for consensus and cooperation among medical specialty groups.

Finally, psychosocial rehabilitation provides an integrative focus for the interdisciplinary care of people with long-term mental illnesses (2, 17). It is what Grob described as "a many-sided and multidisciplinary process" (51, p. 271), and, as such, it is entirely in keeping with the goals set forth for community health as they were expressed in President John F. Kennedy's 1963 statement (9) on a "bold new approach" in mental health service delivery.

These are too many "integrations" to ignore. The field of psychosocial rehabilitation is important to psychiatry—and vice versa—for so many different reasons that it is foolhardy to focus more on differences than on areas of concordance (54). Whether one considers psychiatric treatment and rehabilitation as two separate approaches or as two parts of a single approach in patient care, they need not be viewed as mutually exclusive. To the contrary, psychosocial rehabilitation and psychiatry can be, and must be, blended, a position that is underscored by the fact that a number of conscientious and respected psychiatrists—among them, Douglas Bennett, H. Richard Lamb, Robert Liberman, Dennis McCrory, Arthur Meyerson, John Talbott, and John Wing—are themselves deeply involved in the theory and practice of psychosocial rehabilitation.

A recent review of the literature on rehabilitation outcome supports the notion that psychiatry and psychosocial rehabilitation complement each other's contributions to the improvement of long-term patients' life circumstances. Although this body of research is limited by the absence of common definitions and out-

come measures and although its validity is generally confounded by the interactive effects of psychiatric and rehabilitative interventions, the existing evidence nonetheless points strongly to the conclusion that both disciplines must be integrated "to help patients achieve maximum feasible adaptation" (15, p. 23). I would submit that, together, these disciplines hold the key to realizing the promise of deinstitutionalization, which seems largely to have eluded us for the past several decades.

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The Psychoanalytic Conceptualization of Perinatal Loss: A Multidimensional Model

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Much has been learned about perinatal loss over the past 20 years through clinical investigations and quantitative research. However, a review of studies over the past decade reveals that perinatal loss is increasingly being seen in the same way as a death of any other member of the family, rather than as a unique bereavement. A comprehensive understanding of perinatal loss anchored in a theoretical framework of pregnancy is lacking. This article offers a multidimensional model for examining this loss by applying four psychoanalytic interpretations of pregnancy. 1) From the perspective of pregnancy ushering in the new developmental phase of parenthood, perinatal loss becomes a developmental interference, disrupting a significant milestone as well as causing isolation from peers. 2) In light of the usual recapitulation of earlier conflicts during pregnancy as noted by drive theory, perinatal loss may lead to an intensification of intrapsychic conflicts. 3) Understanding pregnancy as the creation of a specific person in an object relations model highlights the importance of mourning after perinatal death, as well as the need to tend to associated unresolved grief from earlier losses. 4) Finally, a model of narcissism describes how pregnancy reorganizes self-esteem, thereby delineating the intense narcissistic injury and rage that often follow perinatal loss. These multiple frameworks help to explain the many repercussions of this loss as well as to account for individual differences. Research findings are selectively reviewed to support the validity of this model. Conversely, this model may productively guide future avenues for research.

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Over the past 20 years there has been a dramatically increased awareness of the grief that usually follows perinatal loss. However, our understanding of the unique dimensions of perinatal loss and exactly what it means to the bereaved family is often sketchy and incomplete. Many anecdotal reports based on interviews with bereaved parents (usually mothers) richly illustrate the affective nature of this grief—the initial shock followed by hurt, rage, yearning, disappointment, and pervasive guilt—as well as common behavioral manifestations in psychosomatic symptoms of depression (1–6). A growing body of quantitative studies is attempting to determine the variables that predict adaptive versus more pathogenic forms of grieving (7–17). Few studies, however, anecdotal or quantitative, offer a comprehensive theoretical framework in which to anchor clinical observations of affective, cognitive,

and behavioral functioning as well as to direct meaningful research questions suitable for quantitative evaluation. We may know a lot about perinatal loss while understanding very little about what this death means to the bereaved. This article attempts to provide a multidimensional psychoanalytic framework in which to integrate clinical and research findings on perinatal loss. It builds on previous works in this area (18–21) by describing how contemporary psychoanalytic perspectives of developmental stages, drives, object relations, and narcissism may deepen our understanding of perinatal loss and guide research. The article does not offer a systematic review of the empirical literature, which is available elsewhere (18, 22, 23).

In the United States, perinatal loss is generally defined as all reproductive losses occurring between the twentieth week of pregnancy and the first month of life (24), including late-term intrauterine fetal death, stillbirth, and neonatal death. In this article I also view earlier pregnancy losses (i.e., miscarriage, ectopic pregnancy, and termination of pregnancy after learning of severe fetal abnormality) as perinatal losses but do not consider elective abortion, which is distinguished by very different reactions (18).

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RECENT CONCEPTIONS OF PERINATAL LOSS

Early studies of perinatal loss highlighted the failure of physicians and nurses to recognize the usual grief and need to mourn following perinatal death. In his now-classic study, Bourne (25) described how stillbirth was typically regarded as a "non-event" by medical caregivers, who were significantly less able to recall such deliveries than the healthy births they had attended. Throughout the 1970s, investigators decried the failure of medical caregivers, families, and friends to recognize and appropriately respond to perinatal loss (26–30), while they noted how such professional and societal indifference could both intensify parental distress and interfere with the resolution of grief (31–33). Many of these studies considered how being oblivious to parental grief could serve the medical caregiver's defensive needs to deny his or her own grief, disappointment, and/or guilt.

More phenomenologically oriented case reports highlighted how perinatal loss is a unique bereavement, stemming from the incomplete separation of mother and baby and leading to a sense of the loss of a part of oneself (34–36) and an intense investment in fantasy in relating to the unborn child (37, 38). However, perinatal loss was increasingly considered much like the death of any other member of the family (23) in terms of mourning the baby as a distinct other (i.e., object loss) rather than a part of oneself. This became evident in a number of ways in the mounting number of studies in the 1980s. Many quantitative studies began to rely on grief measures developed for other bereavements, such as death of a spouse or child, implicitly not regarding perinatal death as a significantly different phenomenon (8–10, 13). While the earlier descriptive studies of the 1970s highlighted the importance of pregnancy in understanding the meanings of perinatal loss, most studies in the 1980s made scant reference to this particular physical and emotional context. Perinatal loss became subsumed within the grief literature as a specific, though not particularly distinct, death.

An understanding of this kind of death needs to include a greater appreciation of its occurrence at the inception of life. Most researchers recognize, of course, that this death is significantly different from other losses in that the bereaved parents have had no opportunity to identify and get to know their baby, through interactions, as a specific, real person who can be mourned. This fact explains the often crucial value placed on viewing and holding the child for providing memories to facilitate grieving. Zeanah's very thorough literature review (22) noted the failure to distinguish adequately the nature of perinatal loss from other family deaths but provided no discussion of how pregnancy may importantly influence the experience of this loss. This is all the more striking in light of the significant work of Zeanah and associates on the development of parental attachment in the last trimester of pregnancy (39, 40). There is a notable discrepancy between researchers' implicit recognition of how peri-

natal loss is unique and their overt failure to translate that understanding methodologically into appropriate measures and interpretively into the theoretical context of pregnancy.

By 1992 the omission of pregnancy from the meaningful investigation of perinatal loss appeared as striking as the repression of memory (and grief) that Bourne (25) had noted about these deaths more than 20 years earlier. While researchers are now able to regard these losses as being as important as other family deaths, they still tend to overlook the ways in which they are different.

A MULTIDIMENSIONAL APPLICATION OF PSYCHOANALYTIC THEORY

I now offer a broad psychoanalytic orientation to highlight the value of an intrapsychic perspective in appreciating the multiple aspects of perinatal loss and in guiding research. Four distinct psychoanalytic frameworks can be used in understanding the meanings of pregnancy and the impact of perinatal loss. Pregnancy may be interpreted alternatively as a developmental milestone, a revival of earlier instinctually charged conflicts, the creation of a new object relationship, and an enhancement of the self. Similarly, perinatal loss can be understood by each of these frameworks as, respectively, a developmental interference, intensification of earlier conflicts, object loss with particular obstacles to mourning, and multiple narcissistic injuries. By orienting to models of adult development, drives, object relations, and self, different aspects of experience (e.g., self versus other) and levels of conceptualization (e.g., biological versus psychological versus cultural) can be considered.

This dissection of psychoanalysis is similar to Pine's depiction (41) of the four psychologies of psychoanalysis—drive, ego, object, and self. While my dimension of drives combines drive and ego into the generally accepted integration of ego psychology, the additional application of developmental stage highlights the centrality of pregnancy and parenthood as a new opportunity for reorganization and revision (rather than only the repetition of issues and identifications in the earlier developmental stages embedded in the other models). Pine (41) has argued that these dimensions can be viewed alternatively as separate psychologies, with an individual developing a unique life history of each, or as different perspectives on the same phenomena, with an increasingly complex web of interacting links. Similarly, I believe that it is useful to preserve the individual integrity of these dimensions in order to highlight how these diverse aspects of pregnancy and perinatal loss may assume a different hierarchical salience among different people; for some, the developmental interference in one's wish to be a parent may be paramount, while for others the loss of the particular child (or the blow to one's self-esteem) may be central. It is especially important to challenge the common implicit assumption that

object loss is the sole or primary dynamic after all perinatal losses. The unique mosaic of developmental wishes, internalized conflicts, complexion of object representations, and narcissistic needs involved in each pregnancy and its loss makes each an individual experience. The different languages and points of reference each model uses also encourage this differentiation. At the same time, these perspectives can be integrated on a higher conceptual level, demonstrating their mutual reinforcement of broader themes as well as their complementarity (18).

Developmental Model

As a new developmental stage, pregnancy typically precipitates a psychosocial crisis in one's internal constellation of representations, conflicts, and fantasies, which interact with the cultural (and subcultural) changes in identity that are induced by becoming a parent. Both intrapsychic and societal dimensions need to be considered. Psychoanalytic theorists such as Deutsch (42) and Benedek (43) have described the maturational importance of pregnancy as a preparation for parenthood that can help establish a more secure and independent sense of adult identity, rooted, paradoxically enough, in a revived reconciliation with one's early childhood experiences. Bibring and her colleagues (44, 45), more than any other theorists, delineated pregnancy as a crisis, with regression providing the essential opportunity for consolidating earlier conflicts, identifications, and issues in a new organization of the personality. As in adolescence (46), the presence of psychological upheaval and distress typically indicates a regression that may not be an indicator of pathology but a prelude to constructive resolution. Some of Bibring and Valenstein's (45) and Ballou's (47) case illustrations offer good examples of how seemingly disturbed and symptomatic reactions during pregnancy presaged more successful adaptation than had been achieved before. Family theorists (48-50), on the other hand, apply a transactional model in which pregnancy, as a transition to parenthood, alters the balance of marital and gender roles that had been established, leading to new interactional patterns and conflicts. The focus here is not on intrapsychic adjustment but on the accommodation of new role demands with previously set modes of satisfaction, communication, and intimacy.

In his classic study delineating the eight stages of human development, Erikson (51) highlighted the crucial role of generativity, typically—although not exclusively nor even necessarily—realized through parenthood:

In this book the emphasis is on the childhood stages, otherwise the section on generativity would of necessity be the central one, for this term encompasses the evolutionary development which has made man the teaching and instituting as well as the learning animal. The fashionable insistence on dramatizing the dependence of children on adults often blinds us to the dependence of the older generation on the

younger one. Mature man needs to be needed, and maturity needs guidance as well as encouragement from what has been produced and must be taken care of. (pp. 266-267)

This quotation underscores the importance of this particular developmental stage as a distinctly influential period that is not reducible to simply another step in the sequence of drive, object, or self development. Furthermore, it beautifully describes the reciprocal influences between parent and child in parental intrapsychic development, as illuminated by Benedek (52), and foreshadows later studies of infant behavior demonstrating how much infants influence (as opposed to being only affected by) their parents (53). Finally, Erikson (51) clearly indicated how this developmental stage emerges at the crossroads of intrapsychic and social maturation: "Generativity thus is an essential stage on the psychosexual as well as on the psychosocial schedule" (p. 267). Appropriately, *Childhood and Society* is dedicated "to our children's children."

Occurring during pregnancy, perinatal loss is a crisis within a crisis. The heightened vulnerability during such an intensified crisis may tax the woman's coping capacities (i.e., ego resources), thereby increasing the importance of "social support" (a too-often undefined concept). The commonly reported significance of available, empathic, and concretely helpful figures—especially husbands (7, 9, 10, 14) but also professional caregivers (7, 12, 29, 33, 54, 55)—in facilitating a more adaptive recovery from perinatal loss may be based on the increased maternal disorganization during this developmental crisis. Many usual responses to perinatal loss, such as visualizing or hearing a baby, the intense wish to have another baby as soon as possible, and the intolerable pain on being exposed to any and all reminders of babies (1, 23, 56), may be due less to the loss of a particular person than to the major disruption in developmental progress caused by this loss—especially if it is a first pregnancy. Perinatal loss is often a developmental interference that intensifies the desire to get back on track developmentally by having a baby to secure one's parenthood.

In addition to the intrapsychic repercussions of failing to achieve the developmental goals of this stage (i.e., "a pervading sense of stagnation and personal impoverishment" [51, p. 267]), perinatal loss often fosters profound interpersonal exclusion from the activities of childbearing friends and siblings. Deprived of this usual support network, the childless couple must now cope with an increased isolation due not only to the loneliness of grief but also to the additional sense of there being no place for them in a community of families. (While some of this discussion applies to perinatal loss after healthy births, since parenthood is a developmental process not achieved all at once, the developmental implications and interference are likely to be more profound when the loss is the first wanted pregnancy.) The value of a support group in easing the pain and promoting understanding of perinatal loss may not be restricted to the usual goal of facilitating

grief (1, 5, 56–58) but, just as importantly, it may provide a reference group that bereaved parents can join and belong to.

Drive Model

Pregnancy can be considered an instinctual process in both the correspondence of hormonal (i.e., progesterone) production with an introverted oral mode of functioning (59) and the recapitulation of infantile sexuality (i.e., oral, anal, and phallic expression) coinciding with each trimester of pregnancy (42, 44, 60, 61). While the first perspective approaches a purely physiological, biological interpretation linking psychosexual orientation to hormonal production, the second view seems traditionally psychoanalytic in basing psychosexual expression on the interface of biology and psychology through the concept of drive (i.e., libido). The two understandings, however, are united by the centrality of sexuality; the first biological version may be associated with Freud's earlier ambition (and heritage as a neurologist) to create a completely physicalistic paradigm of psychic functioning before he developed the psychological machinery embodied in the libido theory, the structural model, and ego psychology (62, 63).

Many researchers have poignantly captured the intense, quite visceral yearning of the bereaved mother for physical contact with her dead child (23, 37, 38). Peppers and Knapp (1) observed that "mothers say they yearn to embrace their baby; their arms ache to hold the baby; their breasts ache to nurse the baby" (p. 42). The profound and quite literal hunger of the mother to nurture her baby is rooted in the normal oral mode during pregnancy, which has been frustrated and denied by perinatal loss. Intensified deprivation can lead to severe depression, which may be based less on a specific object loss (as most researchers suggest) than on the orally regressed state of pregnancy in which this loss occurs. The mother's powerful need to hold, feed, and care for her child cannot be based on prior memories of those actual interactions (the usual content of grief after object loss) but draws on cherished maternal and infantile wishes fueled by both the regression to the oral subphase within pregnancy and the deprivation caused by the child's death.

The revival of "unfinished business" in pregnancy may invite the bereaved mother to construct distorted, maladaptive understandings of her perinatal loss based on earlier conflicts. There are many psychotherapeutic case examples of maternal perinatal loss becoming linked with earlier, unresolved oedipal conflicts, the bereaved mother's ambivalence toward her own mother, and unresolved separation-individuation issues (18). Although other clinicians have described the benefits of some form of counseling or psychotherapy after perinatal loss (64–68), virtually all of them have focused on the circumstances and importance of mourning this often inaccessible object loss, neglecting much consideration of the internalized conflicts revived by the loss.

Object Relations Model

This perspective highlights the primacy of human relationships with an internal world of object representations guiding motives, epitomized, for our purposes, by Bowlby's model of attachment (69). By the last trimester of pregnancy, an intense attachment to the unborn child as a separate, distinct person usually develops (39, 40, 70–73). This perspective involves, moreover, not only seeking a new object (one's child) but reviving, reclaiming, and reorganizing early object ties, as a baby, to one's mother and, as a mother, identifying with maternal figures both past and present. The handiwork of earlier psychoanalytic theorists such as Deutsch (42), Benedek (74), and Bibring (44) displayed threads of drive and object relations inextricably woven together. More recent investigators have tended to emphasize the centrality, if not primacy, of the earliest relationship with one's mother over the drives in determining the course of pregnancy (47, 75). Sometimes the differences between these two perspectives are highlighted, leading to their definition as divergent orientations, depending on whether controlling the drives or resonating with the other is ascendant (76).

Most theorists focus on how perinatal death is the loss of a cherished, distinct other and recognize how mourning is complicated by the lack of memories and interactions with the dead baby, the lack of professional and familial support for grieving over this loss, and the unexpected suddenness of the death, which often leaves parents feeling confused and disoriented, sometimes doubting the reality of both the pregnancy and the death (31, 32). It logically follows that naming, seeing, holding, and burying one's dead child can significantly facilitate mourning by promoting the creation of a distinct identity for this child as well as by making both the pregnancy and the death more real. Not surprisingly, virtually every researcher who has studied perinatal loss and every clinician who has worked with these parents strongly endorses providing opportunities for parents to make the reality of the dead child be recognized and encourages bonding to the newborn so that it can be more completely mourned (1, 5, 18, 23, 31, 32, 35, 37, 38, 55, 56, 77). However, in focusing exclusively on the loss of this specific child, additional object ties—such as an unresolved parental death in childhood—associated with the pregnancy and now the death of this child are overlooked. There are numerous cases in which depression associated with earlier unresolved grief, especially for a mother or maternal figure who died in childhood, was precipitated by perinatal loss (18). Because pregnancy involves not only seeking a new child but also resurrecting important parental relationships, mourning perinatal loss requires resolving the grief for the child who has died *and* the legacy of past object images conferred upon that child.

Narcissism Model

Just as the fetus is physically a part of the mother, the unborn child initially is experienced much more as

a part of the mother's self than as a separate person. While over the course of pregnancy (and especially at birth) the balance shifts as the child is viewed as an increasingly distinct individual, the mother's narcissistic experience of her child remains throughout that child's life as a vital and unique ingredient of parental attachment. Mothers invest a considerable portion of their self-esteem in the child-to-be. Deutsch (42) observed, "Pregnancy is a welcome opportunity to enhance their own importance" (p. 156). "Often it [the fetus] appears as an ideal child, usually representing the dreamer herself endowed with her own best qualities and all those she would like to have" (p. 162). I have discussed at length (18) how pregnancy fulfills crucial narcissistic ambitions by 1) fostering the achievement of omnipotence, both in the act of creation and in becoming a mother, who is imbued with such power in the mind of a young child, 2) affirming one's femininity through reproduction, and 3) serving as a vital narcissistic defense against death anxiety through a sense of immortality because of one's biological continuity in the next generation. Kohut's concepts (78) may help explain how an expectant mother's self-esteem can be regulated by the experience of her unborn child as a "selfobject" that reflects and confirms (i.e., mirrors) her self-worth and represents (i.e., idealizes) the best part of herself. As Kohut (79, 80) frequently warned, it is crucial to regard narcissism not as a primitive form of object relatedness (i.e., a form of psychopathology) normatively replaced by mutual ties but as a separate line of development that is never relinquished, while it is susceptible, like object relations, to maturational transformations. Studying pregnancy highlights how a mother's narcissistic investment in her unborn child is normal, although the nature of that narcissistic tie may be more or less adaptive (just as it is with the object tie to the child as a separate person).

Many of the reactions to perinatal loss may be more clearly understood by applying a narcissistic orientation than by viewing the loss as solely that of an object (18, 34, 36, 56, 77). Furman (35) poignantly described how many of the usual responses to perinatal loss—the emptiness, low self-esteem, and unbearable helplessness—emanate from this loss of part of the self. Since a selfobject, by definition, is experienced as an extension of oneself over which one has complete control (78), we can better understand the profound helplessness so often voiced after perinatal loss and why this is so intolerable in light of the omnipotence that pregnancy is meant to secure.

The underlying shame and feeling of inferiority resulting from narcissistic injury are particularly painful, likened to the experience of amputation (35) or the frustration of brain-injured patients (80). The pervasive low self-esteem—sense of inadequacy, failure, and worthlessness—following perinatal loss is less convincingly explained by the process of mourning an object loss than by the consequences of narcissistic damage and the inability of the deceased child (i.e., selfobject) to support maternal self-esteem. LaRoche et al. (9) re-

ported that although measures of bereaved mothers' depression and mourning showed a statistically significant and positive association, the degree of mourning for the dead child could account for only about 20% of the extent of depression. Perhaps the multiple narcissistic assaults on the mother's self-esteem contribute more powerfully to her depression than does the loss of her baby as a distinct object. Common psychosomatic manifestations after pregnancy loss, especially the sense of inner emptiness, of unreality, and of hearing a baby, may be rooted not only in the usual depressive symptoms and the physiological residues of pregnancy but in the fragmented experience of the self and the similar somatic complaints expressed by those coping with narcissistic assault (78).

The insensitivity of professional caregivers, family, and friends to parents experiencing perinatal loss has already been well documented. However, the fury provoked by this lack of understanding by others may be better appreciated by recognizing how narcissistic rage (80) is ignited by such personal injuries. The maliciousness sometimes attributed to insensitive or indifferent others may be based not on the degree of actual meanness shown but on the narcissistic vulnerability of these bereaved parents to slights. This statement is not intended to excuse professional or familial insensitivity, or to suggest that it is necessarily a misperception, or to pathologize this narcissistic vulnerability. Rather, it highlights the importance of empathic communication with these parents and how they may experience genuine slights as frontal assaults. Not understanding and misinterpreting their pain becomes a fresh stab in an open narcissistic wound. The high rate of litigation against obstetricians is probably not due to the poorer performance or greater insensitivity of these physicians. Seeking vengeance in a lawsuit in the heat of narcissistic rage that may have been fueled by a callous professional attitude seems a more convincing explanation.

Kohut described how, in the psychoanalysis of chronic narcissistic character disturbance (78) and less pervasive narcissistic problems, which he later claimed permeated virtually all emotional problems (79), the therapist's empathic bond facilitates the slow process of building a reliable, internalized self structure that can now regulate self-esteem without depending as desperately on the selfobject transference. The typical regression to greater narcissistic vulnerability in response to loss may be repaired in an empathic bond in short-term psychotherapy (18). Quantitative evidence for the value of empathic understanding in promoting narcissistic recovery may be provided by Murray and Callan's report (12) of parents expressing significantly higher levels of self-esteem when they were satisfied with support received from hospital staff members. Perhaps Furman (35) said it best and most clearly: "For the professional person to tell the parents just to bear it is not enough; to be with them and to extend oneself in bearing it can do much more. It is this, in part, which makes the job of working with these parents so difficult" (p. 216).

IMPLICATIONS FOR RESEARCH

Although the multidimensional psychoanalytic model proposed here is based on a study of 20 bereaved mothers evaluated for or in psychotherapy (18), it may productively guide quantitative research on perinatal loss to test specific hypotheses. There is an increasing trend toward the use of regression equations based on a wide net of independent variables in attempting to predict a "pathological" outcome, without the application or evaluation of any guiding theoretical model (8, 10-12, 14, 15). While significant results are inevitably discovered and thoughtful conclusions sometimes drawn, rarely are they meaningfully organized into a conceptual framework. As investigators have repeatedly indicated (14, 22, 23), differing results among studies (e.g., the effects of previous losses and births, length of gestation, etc. on the impact of perinatal loss) may have been significantly influenced by widely varying methodology, such as what perinatal losses were assessed, the nature of the sample, and how long after the loss measures were administered. Most researchers adhere to the prevailing model of object loss, comfortably using measures of mourning designed for other bereavements such as the death of a spouse (8-10, 13) and thereby disregarding important developmental, narcissistic, and conflict-related effects of perinatal death that would go undetected by these limited measures.

The construction of measures specifically oriented to perinatal loss is encouraging. The Perinatal Grief Scale (14, 15) has distinguished three distinct factors: active grief, difficulty coping, and despair. While active grief seems to be associated with mourning an object loss (e.g., "I am grieving for the baby," "I can't avoid thinking about the baby," and "I very much miss the baby"), despair appears to index narcissistic damage, including low self-esteem (e.g., "The best part of me died with the baby," and "I feel worthless since he/she died"), psychosomatic symptoms ("I feel physically ill when I think of him/her"), and a sense of emptiness ("It's safer not to love," and "I try to laugh, but nothing seems funny anymore"). This work appears to illustrate nicely how mourning object loss and incurring narcissistic injury are relatively independent aspects of perinatal loss.

Many studies readily equate the expression of intense grief with inadequate coping or unresolved grief (8, 10, 16, 17), even as early as 8 weeks after the death (11), when such intense grieving is to be expected. This suggests how deeply ambivalent researchers are toward the normalcy of intense grief after perinatal loss. While this grieving is repeatedly regarded as typical and is encouraged by providing opportunities to see and hold the dead baby, when it is empirically studied, intense grief, even soon after the death, is often viewed as pathological! Lasker and Toedter (15) recently reported that their factors of difficulty coping and despair were more significantly associated with chronic emotional problems 2 years after the loss than was active grief, which convincingly argues against equating the intensity of grief with problems in recovering from perinatal loss. Al-

though Theut et al. (16, 17) clearly recognized the importance of narcissistic loss, their Perinatal Bereavement Scale unfortunately focuses almost exclusively on mourning object loss, with questions on the death of the baby rather than diminished self-esteem. Their results revealed more intense and prolonged grieving for a late-term loss than for a miscarriage, a frequently reported finding (23) that is not surprising in light of the increasing attachment to the unborn child as a separate person as pregnancy advances. Toedter and Lasker (14, 15) confirmed this expected finding, reporting that the gestational age of the unborn child was more strongly associated with active grief (i.e., mourning object loss) than with their other two factors.

While it will be a challenge to quantify intrapsychic variables, at least some measures of overall psychological functioning and coping are necessary, lest it be assumed (as some studies appear to do) that the impact of perinatal loss is solely determined by the circumstances of the loss and environmental factors (which, of course, are more readily assessed). Kellner et al. (81) have indicated that demographic and obstetric characteristics are in fact poor predictors of parental reactions and decisions after perinatal loss, a finding emphasized by Lasker and Toedter (15) in their consideration of long-term consequences. On the basis of their empirical investigation of perinatal loss, Smith and Borgers (13) similarly concluded that "it is not the particular variables of the loss experience which influence the grief response as much as the individual personality variables and the perception that the loss experience is not understood or supported by family and community" (p. 212). The different psychoanalytic models that I have outlined should be evaluated by measures of perinatal loss. The developmental model would predict that perinatal loss before a successful birth will generally be more difficult to endure—a recently reported finding by Lasker and Toedter (15)—because of the greater interference in development and isolation that these parents have to bear in comparison with those who have attained parenthood before such a loss.

Psychoanalytic studies of clinical subjects typically reveal that prior disturbance, unless treated, leads to maladaptive outcome in pregnancy (42, 82), and it seems reasonable to expect that this relationship would be at least as powerful under the additional stress of perinatal loss. Lasker and Toedter (15) in fact discovered that prior mental health problems were the most powerful predictor of enduring emotional problems 2 years after the loss. It is especially valuable not to rely on clinical studies that will be oriented to psychopathology but to consider psychoanalytic investigations that use untreated subjects, such as those conducted by Bal-lou (47) and Bibring (44, 45). Their subjects suggest an important resourcefulness and potential for new adaptation during pregnancy, without treatment or with limited supportive intervention, even among those struggling with prior conflicts. The individualized ways in which parents memorialize their deceased babies (18) illustrate the possibility of creative outcomes in the

mourning process, as described by Pollock (83, 84). Clinical case studies provide an in-depth perspective that is rarely available in research interviews, but they cannot replace untreated samples, which, while evaluated psychoanalytically, may be less susceptible to a bias toward pathology. In developing indexes of intrapsychic functioning, it will be important to consider ego strength as well as disturbance.

Research should assess more precisely the meaning of the pregnancy loss in light of the mother's history. While many studies report no significant association between prior losses and the impact of perinatal death (7, 10, 13-15, 54), no study has examined the possible relation between resolution of earlier losses and subsequent perinatal death, thereby obscuring the impact of earlier losses (12, 22). Furthermore, even if no significant effects on grieving are uncovered, this does *not* mean that earlier losses are inconsequential. In his richly illustrated nonquantitative study of pregnancy following a stillbirth, Phipps (85) described how mothers may typically guard against another feared loss by muffling their attachment to the next child during pregnancy and for some time after birth. More intense grief, which one might expect if an additional perinatal loss should occur, may thereby be avoided. In these instances, a previous perinatal loss may have a significant impact on the mother, albeit not detected by a simple quantitative scale of grieving over object loss.

The qualitative dimensions of depression evoked by perinatal loss must be more carefully distinguished as well as calibrated. It is no longer adequate to apply a global measurement of depression as indicative of unresolved grief; dimensions of grief are not effectively assessed by indexes of depression only (9, 14, 15). A certain degree of behavioral self-blame, in which the bereaved parent believes that future losses may be prevented by specific actions, may engender a sense of mastery and control, limiting the traumatic helplessness that often follows such a loss; this is suggested by empirical findings supporting the defensive-attribution hypothesis (86-88). This guilt, inoculating the bereaved against a more debilitating powerlessness, must be conceptually and methodologically distinguished from the feeling of worthlessness resulting from narcissistic damage, which, while common, is not adaptive. Very different questions would distinguish a mother blaming herself for behavior during her pregnancy that she could change in the future and a mother experiencing a pervasive sense of failure. There is also a crucial difference in affective tone; self-blame regarding behavior potentially provides hope and the possibility of efficacy for the future, while narcissistic devaluation intensifies despair and inadequacy.

Finally, the impact of perinatal loss on the father should be studied more carefully and distinguished along these dimensions. This article has focused on maternal reactions. However, fathers grieve after perinatal loss, although with reportedly less intense and sustained guilt and depression than do mothers (11-13, 16, 17, 32, 54). While the differing biological participa-

tion of men and women in pregnancy might suggest more profound object and narcissistic losses for mothers than fathers, this is subject to individual variation. Perinatal loss may be expected to precipitate developmental interference and revived conflicts in men, just as in women. The research literature may exaggerate how differently men and women respond to perinatal loss, obscuring how similar their coping reactions may be (89). I have dealt with the complicated dynamics of perinatal sibling loss elsewhere (18, 19, 90).

CONCLUSIONS

Over the past 20 years, we have come to appreciate that perinatal death usually means the death of a baby. We now need to consider more thoughtfully how this death has other implications as well for a parent's self-esteem, developmental goals, and ability to cope with earlier conflicts. A multidimensional psychoanalytic model can assess how perinatal loss causes developmental interference, intensifies chronic conflicts, presents particular challenges to mourning an object loss, and inflicts narcissistic damage. This multifaceted paradigm may help account for individual differences as well as explain the multiple effects of perinatal loss on the bereaved parents. Not only may this perspective improve the development of clinical interventions (18) but it may productively guide research—suggesting important and meaningful questions and providing a conceptual framework in which to interpret results and a means of testing and refining the theoretical system. Psychoanalytic insights and hypotheses should be more systematically used not only in the familiar terrain of case studies but in quantitative investigations of perinatal loss as well.

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Contested Boundaries of Bipolar Disorder and the Limits of Categorical Diagnosis in Psychiatry

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The authors' primary objective is to outline the phenomenology, importance, and available data on issues concerning the boundaries between bipolar disorder and diagnoses such as schizophrenia, unipolar depression, and personality disorders. In addition, by illuminating the many difficulties with the boundaries of one of psychiatry's more robust diagnoses, they hope to awaken in the reader a healthy skepticism about current psychiatric nosology. For a topic of this scope, a literature review must be selective. For each boundary area, a mixture of classic and recent papers covering a range of validating criteria is included whenever possible. Good summary data are cited when available, as are a selection of relevant theoretical papers. The review indicates that current diagnostic criteria for bipolar disorder are generally reasonable, but there are many problem areas, most of which cannot be solved by changes in criteria. Notable among these are 1) the possibility of future manic episodes in unipolar disorder, 2) schizoaffective disorder, bipolar type, and 3) borderline personality disorder with prominent mood swings. The disputes concerning the boundaries of bipolar disorder illustrate the limitations of categorical diagnosis which result from the implementation of diagnostic criteria, the criteria themselves, the fundamental nosologic process, and the phenomena themselves. If these limitations are to be extended, it may be necessary to explore alternative ways of defining psychiatric diagnoses for different settings in research and clinical practice.

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Bipolar disorder, by virtue of its fairly distinct phenomenology, its occurrence throughout history (1) and across cultures (2), its patterns of inheritance (3), and its clear disturbance of physiologic function (4), can lay claim to being one of psychiatry's most robust diagnostic entities. Because the readily recognizable core phenomenology—episodic highs and lows and a normal baseline in between—may be absent or obscured by other symptoms, the diagnosis is often difficult to make in practice (5), even by using the relatively narrow and explicitly defined *DSM-III-R* criteria. Some of the ambiguity has to do with operationalizing the

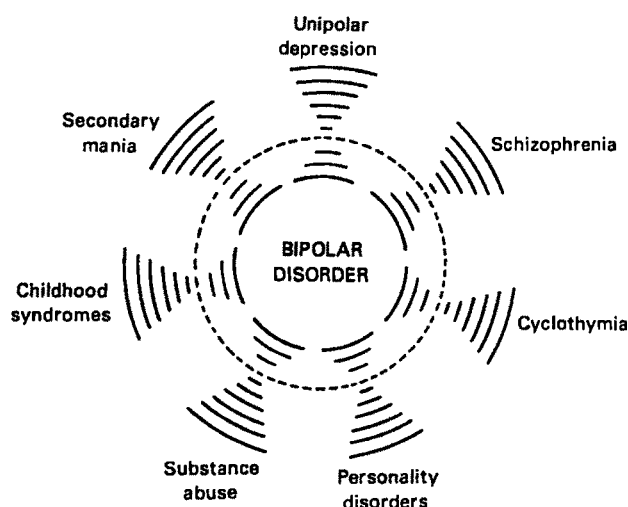
criteria and is usually in the form of unreliability. Such issues, while critical (6), are generally beyond the scope of this essay. Our primary concern is the *validity* of the criteria, particularly as they distinguish bipolar disorder from other psychiatric syndromes.

We begin from the premise that there is a valid diagnostic entity called bipolar disorder, the center of which is well-defined and well-recognized. Clinical experience tells us that symptoms of bipolar disorder overlap substantially with those of other psychiatric disorders. As the patient becomes more psychotic, particularly as symptoms become more chronic, we wonder about schizophrenia. As manic symptoms become less prominent or are absent altogether, we wonder about unipolar disorder. If a substance-abusing patient has mood swings, we wonder if they are drug-induced or whether drugs are masking more dramatic affective episodes. As a framework for this discussion, we have chosen to think of each of these alternative diagnoses as defining a boundary of bipolar disorder, as represented in figure 1. We do not mean to imply that the alternative diagnoses do not overlap with one another, nor do we mean that individual patients can be mapped onto this diagram. Indeed, in the clinical setting, the most difficult patients tend to straddle several of these boundaries. However, most of the interesting nosologic questions *can* be mapped onto the diagram: bipolar II disorder on

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FIGURE 1. The Boundaries of Bipolar Disorder



the boundary with unipolar illness, schizoaffective disorder on the boundary with schizophrenia, and so on.

Our primary aim is to review each of these boundary areas. After a brief description of a boundary's phenomenology and importance in practical and theoretical terms, we go on to review the available data and draw reasonable—sometimes tentative—conclusions. We have tried to cover a wide range of issues within the constraints of available space but have made depth of discussion a function of the importance of the issue in question. In choosing evidence, we have been guided by the standard validating criteria for psychiatric nosology outlined by Robins and Guze (7). However, we agree strongly with Kendler (8) that evidence from different validating criteria may be in conflict and that certain criteria may make more sense in certain settings.

We do not, in general, aim to suggest improvements in criteria for bipolar disorder in *DSM-IV*. No matter how we define criteria, considerable ambiguity about where and whether to draw lines between bipolar disorder and other disorders will remain. Many questions transcend the revision of diagnostic criteria; different criteria may be appropriate for different purposes (8), and some questions can only be answered probabilistically. Thus, we are concerned at a more theoretical level with how we can decide what should and should not be classified with bipolar disorder in a given setting.

These general issues point to our secondary aim. The boundary issues concerning bipolar disorder are by no means unique. Instead, they illustrate a broad range of critical theoretical issues for diagnostic boundaries. Indeed, diagnostic ambiguity is much more serious for many disorders defined in *DSM-III-R* and will no doubt remain so with the publication of *DSM-IV*. There are distinct limits to our ability to draw lines between disorders on the basis of phenomenology alone. At least for some psychiatric disorders, discrete categories may be an illusion. A number of papers have raised some of these concerns (8–11), yet few have done so in

the context of a specific diagnosis. By grounding our discussion in one of psychiatry's best-characterized disorders, we hope to underscore deeper difficulties with current psychiatric classification systems.

THE UNIPOLAR-BIPOLAR DISTINCTION

The phenomenology at the boundary between unipolar and bipolar disorder is one of nested symptoms; i.e., all of the symptoms of unipolar disorder are within the definition of bipolar disorder. Because anyone with unipolar disorder could go on to have a manic episode and be diagnosed retrospectively as bipolar from the first onset of depression, the diagnosis of unipolar disorder must be provisional, at least through the broad age range of susceptibility to mania. Given an episode of major depression, bipolar II disorder (depression plus hypomanic episodes) lies on a continuum with bipolar I disorder (for which manic episodes are required) and thus raises a different set of issues.

Ambiguities at this boundary are critical, in large part because unipolar disorder is vastly more prevalent than bipolar disorder. In addition, unipolar disorder is more difficult to distinguish from normal mood changes, and estimated prevalence rates vary widely depending on duration, severity, and the required number of symptoms (3). Also, unipolar disorder is clinically and probably etiologically more heterogeneous than bipolar disorder (12). Finally, the distinction is central to the current understanding of mood disorders.

The Current Boundary

Support for drawing a boundary between unipolar disorder and bipolar disorder is far too extensive to detail here. The distinction is validated to an extent by each of the classic criteria (7), but in all cases there is substantial overlap, which, as several investigators have pointed out, is equally compatible with continuum models (13, 14). It must be noted, however, that true differences are probably larger than those observed: because of the possibility of a later manic episode, samples of unipolar subjects inevitably contain some bipolar individuals.

Epidemiologic studies show consistent differences between unipolar and bipolar disorder in sex ratio, age at onset, and frequency of affective episodes (4). Depressive episodes in bipolar disorder appear to be more severe (15), even psychotic (16), and to have so-called reverse neurovegetative signs (17). Follow-up data suggest that between 5% and 20% of unipolar patients switch to a bipolar course (18–21).

The genetic data are equally complex; they have been summarized by Tsuang and Faraone (3). In general, bipolar disorder shows clearer genetic transmission than unipolar disorder. Only a few studies of the relatives of unipolar probands have shown a significantly greater prevalence of bipolar disorder than in the relatives of control probands, but most studies of the relatives of bipolar probands have shown a two- to threefold in-

crease in the prevalence of unipolar disorder (14, 22). The increase in unipolar disorder in the relatives of bipolar probands tends to diminish, however, if three or more episodes of depression are required for a diagnosis of unipolar disorder (3). However, evidence varies, as do interpretations, and there are not enough data to decide unequivocally between continuum and separate disorder models.

As for response to treatment, bipolar disorder appears to be more responsive to prophylactic lithium (23), but the differences may have been overstated (24, 25). Antidepressant treatment may be more likely to cause manic symptoms—or full-blown manic episodes—in bipolar patients (26), but this too is controversial (27, 28), and the reasoning can sometimes be circular, since some researchers use pharmacologically induced hypomania as a marker for bipolar disorder (20, 21).

There is some evidence that subjects with unipolar and bipolar disorder differ on a number of laboratory measures, such as neurotransmitter metabolites and neuroendocrine response (4). However, in addition to the lack of robust, replicable differences, much of this evidence suffers from failure of studies to distinguish between state and trait (comparing depression and mania rather than unipolar disorder and bipolar disorder) or to control for the effects of activity level, sex, age, and so on (13).

"Potential Bipolar" Individuals

What are sometimes called false unipolar individuals (3, 4)—those who currently have unipolar depression but will go on to have a manic episode—pose the most intractable difficulties on this boundary. No set of criteria can tell us which unipolar individuals should be considered bipolar for research or clinical purposes. Given a crystal ball, one could limit oneself to the 5%–20% who will actually manifest mania. Consistent with unipolar-bipolar differences, the highest rates are reported for younger (21) or more severely depressed (18) samples, although longer follow-up time (18) and less stringent criteria for mania (20) must also play a role. Similarly, the unipolar individuals who switch at follow-up are younger, include more males, and have more severe episodes, and they may have more prior episodes, earlier age at onset, and certain specific symptoms (20, 21, 29).

Data about these "switchers," however, tell us only about unipolar subjects who actually manifest mania; there must be individuals who share the bipolar genetic liability but for some reason (e.g., variable expressivity of a putative gene for bipolar disorder, absence of environmental or genetic cofactors, competing risks) never have a manic episode. This group is more theoretical and therefore cannot be clearly quantified, much less profiled. According to the most conservative definition, it is limited to those individuals who die (e.g., by committing suicide) during or after an episode of depression and before what would be their first manic episode. According to the most extreme definition, it could include

all unipolar individuals and therefore be equivalent to denying the unipolar-bipolar distinction.

However they are defined, "potential bipolar" individuals constitute some fraction of those diagnosed as having unipolar disorder. Failure to take this into account is probably responsible for at least some of the confusion besetting genetic, physiologic, and treatment studies of the unipolar-bipolar distinction. Some authors have suggested using family history of mania as a way to distinguish which unipolar individuals should be considered as potentially bipolar, and have even suggested that unipolar individuals with family histories of bipolar disorder be called bipolar III (12, 30). Using this criterion in conjunction with the observed characteristics of "switchers" may be of some help for clinicians' informal weighing and balancing, but it is unlikely to be adequate for most research purposes. Family history is particularly problematic within the context of genetic research, since unipolar disorder is so common that some relatives with unipolar disorder would be found in the families of bipolar probands by chance.

The Status of Bipolar II Disorder

Bipolar II disorder (classified in *DSM-III-R* within the category of bipolar disorder not otherwise specified) could be part of unipolar disorder or bipolar disorder, could represent a valid diagnosis in its own right, could be the midpoint on a continuum, or could simply be useful as a buffer zone. Studies of bipolar II disorder have been limited by variable definitions (31) and the well-documented difficulties in assessing hypomania (19).

The data on bipolar II disorder suggest that it is more similar to bipolar I disorder than to unipolar disorder in demographics and course of illness: there is a fairly early age at onset, males are represented more nearly equally, and episodes are more frequent, more severe, and more likely to have reverse neurovegetative signs (30, 31), but such findings are not universal (32). Family studies tend to show that bipolar II disorder is more like bipolar I (12, 31). However, the greater rate of bipolar II disorder in the families of probands with bipolar II disorder suggests that bipolar II may be, at least to an extent, a genetically separate syndrome (31). In addition, there is some evidence that bipolar II disorder is more likely than unipolar disorder or bipolar I disorder to occur with other psychiatric diagnoses, including personality disorders and substance abuse (31). This comorbidity, along with the inconsistencies in the other findings, may be an indication that bipolar II disorder is heterogeneous and includes some true bipolar individuals, some unipolar individuals with other problems that are easily confused with hypomanic episodes, and some individuals with multiple diagnoses.

SCHIZOPHRENIA VERSUS BIPOLAR DISORDER

The boundary between bipolar disorder and schizophrenia involves not a true continuum of purely quan-

titative changes but, rather, varying admixtures of features thought to cluster in one disorder or the other. Much of the dispute has centered on the definition and interpretation of schizoaffective disorder, a diagnosis for those patients whose psychotic symptoms are not clearly linked to their affective episodes. Fewer data are available for two other related disorders, schizophreniform disorder and brief reactive psychosis, so our discussion will concentrate on schizoaffective disorder.

Although the number of potentially misclassified patients is smaller here than at the boundary with unipolar disorder, it is large enough to pose significant practical problems. In addition, because the relation between cross-sectional symptoms and course of illness is critical to the modern understanding of bipolar disorder, this boundary is of great theoretical interest.

The Schizophrenia-Bipolar Split

Despite the similar demographic features, clinicians and investigators have no difficulty distinguishing the phenomenology of classic schizophrenia and classic bipolar disorder, particularly if they have access to longitudinal as well as cross-sectional information. Unlike schizophrenia, classic bipolar disorder is episodic, its episodes are marked by affective and neurovegetative changes, and its psychosis is linked temporally and thematically with mood (*DSM-III-R*). However, religious and paranoid delusions or hallucinations, catatonia, and incoherence can be seen in both disorders, and certain other features said to be typical of one or the other (*DSM-III-R*) involve very subtle distinctions—between inappropriate and labile affect, between flight of ideas and looseness of associations, and so on.

Of course, many patients do not present a classic picture; a substantial minority of patients are difficult to place on one side of the boundary or the other. The findings of Brockington et al. (33) are consistent with clinical experience: in their discriminant function analysis, a general psychotic sample conformed to a bimodal distribution, but, not surprisingly, a sample of schizoaffective patients did not. Some have argued that the very existence of patients with schizoaffective disorder is strong evidence for a continuum of psychotic disorders, or even a unitary psychosis (34), but the data are compatible with a number of other explanations.

On the whole, the distinction between bipolar disorder and schizophrenia appears stable over time. A few follow-up studies have found changes from schizophrenia to bipolar disorder, or vice versa, in a modest fraction of patients (35), but these may represent initial misdiagnosis due to overreliance on cross-sectional symptoms. As for the relation between cross-sectional symptoms and outcome, despite the classic descriptions, it is well-known that some schizophrenic patients do well (35, 36), and some bipolar patients develop chronic courses (37). Kendler et al. (38) raised the possibility that poor outcome is observed more frequently in schizophrenic patients simply because past chronicity (required for the diagnosis of schizophrenia) predicts

future chronicity, but they found in their review that course was fairly strongly associated with cross-sectional symptoms: 6 months of symptoms predicted a poor outcome *only* in patients with index symptoms of schizophrenia, not of bipolar disorder.

Family data tend to support separate inheritance: each of the classically defined disorders "breeds true" to a substantial extent (3, 4). Only small increases in bipolar disorder—usually not statistically significant—are reported among the relatives of schizophrenic subjects when they are compared to relatives of control subjects (22, 39, 40), and the same is true for schizophrenia among the relatives of bipolar subjects (14, 22, 41). This very modest "heterotypic risk" may be consistent with classification error, as demonstrated by Kendler (42).

Fairly robust differences in response to treatment have been observed. Lithium is not generally helpful for patients with schizophrenia, while it decreases the severity and duration of individual episodes and is prophylactic against further episodes in patients with bipolar disorder (43). Of course, both disorders (and many others with psychotic features) tend to respond to neuroleptics, but this is rarely used as an argument for the unity of psychotic disorders.

Physiologic and anatomic data on the two disorders as classically defined do show some differences, but none is robust enough to serve as a biological marker. Structural abnormalities are more frequently reported in schizophrenic individuals, but they have also been found in many bipolar subjects (4). Functional abnormalities, including changes in sleep architecture, endocrine responsiveness, and catecholamine metabolites, are more easily demonstrated for bipolar disorder (4). However, it is difficult to know to what extent these are simply the physiologic manifestations (state markers) of increases in activity in the manic state.

On the whole, there is considerable support for the clinical and research utility of separating bipolar disorder and schizophrenia. Although the unitary psychosis model is difficult to disprove, the differences observed—despite dilution due to at least some misclassification—and the fairly low prevalence of schizoaffective disorder compared to bipolar disorder and schizophrenia lend support to the two-major-psychoses model. Especially in the complex boundary zone, however, much work remains to be done.

What Is Schizoaffective Disorder?

Like bipolar II disorder, the schizoaffective diagnosis was created as a buffer zone, and similar questions apply. Studies of schizoaffective disorder must be read and compared with particular care, since the term has been used with a variety of meanings. The Research Diagnostic Criteria (RDC) subtyped schizoaffective disorder on the basis of mania versus depression and mainly affective (mood-incongruent psychosis *within* a mood episode) versus mainly schizophrenic (psychosis *between* episodes) (44, 45). Although not everyone agrees

(46), these distinctions appear to make a difference. First, schizoaffective depression may be more common (45) and appears to differ more from the corresponding mood syndrome than does schizoaffective mania, especially within the mainly affective subtype (47–49). The mainly affective subtype appears to be more similar to mood syndromes, especially within the manic or bipolar group (40, 47–49). Because several studies found RDC-defined schizoaffective mania to be virtually indistinguishable from bipolar disorder on a number of validating criteria (at least in the mainly affective subgroup, which probably predominated in these studies) (47, 48), the *DSM-III* criteria for mania were broadened to allow more psychosis within individual episodes. Although this change has remained somewhat controversial, the similar changes made for depression are far more problematic (35, 45).

We have tried to limit the discussion to studies that have reported specific information on *DSM-III-R* schizoaffective disorder, bipolar type (or the nearly equivalent RDC mainly schizophrenic subtype of schizoaffective mania). However, because narrowly defined schizoaffective disorder as a whole is fairly uncommon, such studies are quite rare. As would be expected from the diagnostic criteria, schizoaffective disorder, bipolar type, has a course and outcome between those of bipolar disorder and schizophrenia (35). Family studies are perhaps the most confusing and the least likely to report separate data. In general, modest increases in bipolar disorder are seen in the families of individuals with schizoaffective disorder, bipolar type, but there are more substantial increases in schizophrenia in these families (40). Few studies have found increases in schizoaffective disorder, bipolar type, itself in the families of probands with the disorder, and thus there is little support for the separate disorder model (49, 50). Studies of response to treatment suggest that lithium may help some patients with schizoaffective disorder, bipolar type, but probably not to the extent that it helps patients with bipolar disorder (50). Of course, lithium's specificity may be for affective (particularly manic) symptoms rather than for bipolar disorder per se. Physiologic studies have found no differences that consistently separate schizoaffective disorder from bipolar disorder or schizophrenia (49).

Given the paucity of specific data, it is no surprise that investigators have been unable to reach consensus on the status of schizoaffective disorder, bipolar type (4, 51). Under these circumstances, it seems wise to maintain schizoaffective disorder, bipolar type, as a buffer zone. As a disorder in its own right, it has little a priori appeal, and almost no data support it. As Levitt and Tsuang have argued (50), schizoaffective disorder is likely to be quite heterogeneous. Schizoaffective disorder, bipolar type, probably includes some individuals who belong in one of the adjacent categories, but it may also include many individuals with organic or other as-yet unrecognized psychotic disorders that do not fit the picture of bipolar disorder or schizophrenia. We may be able to refine the diagnosis of schizoaffective

disorder, bipolar type, by pooling data from older studies and exploring which subtyping schemes are predictive of differences in outcome, treatment, and familial relationships.

CYCLOTHYMIA

The boundary of bipolar disorder with cyclothymia—the term is used here to denote formal *DSM-III-R* cyclothymia along with any other syndrome made up of minor highs and lows—is on a true continuum with bipolar I disorder and bipolar II disorder. Cyclothymia is rarely defined specifically; rather, it refers to a syndrome made up of episodes resembling depression and mania but of insufficient severity, duration, or number of symptoms to meet the criteria (*DSM-III*, *DSM-III-R*, 52). Thus, it is by definition, if not in fact, a mild form of bipolar disorder. While *DSM-III* and *DSM-III-R* add a chronicity requirement (no more than 2 months at a time can be symptom free), this definition has not been applied consistently in the literature.

Understanding the relation of cyclothymia to bipolar disorder has considerable practical implications, since the syndrome appears to be at least as common as bipolar disorder. In addition, because cyclothymia exists on a continuum with bipolar disorder at its upper boundary and with normal mood swings at its lower boundary, it may contribute to an understanding of some of the positive aspects of bipolar disorder and related phenomena (4).

While the nature of cyclothymia's relation to bipolar disorder remains unclear, the fact of a relationship seems well-established. By definition, the phenomenology is closely linked. Mood swings per se may not be unique to bipolar and related disorders, since Fichtner et al. (53) found them as often in schizophrenic as in bipolar individuals. Nonetheless, cyclothymia itself does cluster with bipolar disorder and not with schizophrenia. Clinicians frequently note that many patients with bipolar disorder have a history of antecedent cyclothymia, and Akiskal et al. (52) confirmed this on a prospective basis in a group of outpatients with cyclothymia. With the exception of Andreasen et al. (47), who reported very low rates of cyclothymia in relatives of probands with all subtypes of affective disorder, nearly all family studies support a relationship between cyclothymia and bipolar disorder. Bipolar disorder is increased in the relatives of cyclothymic patients (52) and cyclothymia in the relatives of bipolar patients (14, 41, 54). There are also a few reports of decreased mood swings when cyclothymic patients are treated with lithium (43, 52). In addition, Akiskal et al. (52) reported a substantial incidence of hypomania in cyclothymic patients during treatment with antidepressants.

There seems to be little doubt that at least some fraction of cyclothymic individuals should be considered to have a variant of bipolar disorder, at least for some purposes. However, particularly if very lax criteria are used, a number of patients with normal mood swings or con-

ditions mimicking hypomania may be included inadvertently. Impairment or hospitalization makes sense as a cutoff point between the diagnoses in clinical settings but not necessarily elsewhere. There is no evidence that the chronicity requirement in *DSM-III-R* helps to distinguish the fraction of cyclothymia related to bipolar disorder (either by outcome or familial connection) from a more generic type. If suitable numbers of subjects could be found, research aimed at elucidating which characteristics predict a relation to bipolar disorder would be most helpful.

PERSONALITY DISORDERS

The boundary of bipolar disorder with personality disorders concerns *DSM-III-R* cluster B, including especially borderline but also histrionic and narcissistic personality disorders. The phenomenology is one of overlapping symptoms. Borderline personality disorder shares affective instability, impulsivity, and transient psychosis with bipolar disorder; histrionic personality disorder shares flamboyance, emotional shifts, and low tolerance of frustration; and narcissistic personality disorder shares grandiosity (*DSM-III-R*). Furthermore, as *DSM-III-R* notes, the boundaries of personality disorders themselves are not very clear; individuals often have features of more than one personality disorder (especially within the same cluster), which only makes the differential diagnosis with affective disorders more difficult. Co-occurrence of personality and affective disorders, possibly including bipolar disorder, raises additional concerns at this boundary.

In addition to the impact of the issue on clinical practice, the relation between personality and affective disorders has profound implications for our understanding of the axis I versus axis II model in our diagnostic system. Despite the atheoretical stance of *DSM-III-R*, there is a tendency to view affective syndromes as being biological or genetic in origin and personality syndromes as being interpersonal or historical in origin, while the truth is probably far more complex. For instance, cyclothymic, hyperthymic, and dysthymic temperaments (which were formerly classified as personality disorders) clearly are related to both mood syndromes and personality.

Despite the intense clinical and research interest, there are only limited data about the relation between personality disorders and bipolar disorder, and they mostly concern borderline personality disorder. There is evidence for increased major depression in borderline patients, and Akiskal et al. (55) have reported increases in bipolar II disorder and cyclothymia as well. In addition to co-occurrence, there may be a "switch" to a diagnosis of mania or hypomania in some individuals initially diagnosed as having borderline personality disorder (55). Family data are unclear. While Akiskal et al. (55) reported some increase in bipolar disorder among relatives of borderline patients, Pope et al. (56) saw increases in depression only, and these may be clustered

in the relatives of borderline patients who themselves have affective disorders. Rates of borderline personality disorder are not reported in most family studies of affective disorders (14, 22, 41, 47, 54), but Coryell and Zimmerman (57) did not see significant increases in borderline or other cluster B personality disorders in relatives of patients with major depression. While there are anecdotal reports of borderline patients improving with either carbamazepine (58) or lithium (59), it is difficult to support a relationship on this basis.

DSM-III and *DSM-III-R* draw a clear boundary between mood disorders on axis I and personality disorders marked by mood *instability* on axis II. Akiskal and colleagues (55, 59) have proposed blurring this boundary, at least for borderline personality, and argue that a substantial fraction of patients diagnosed as borderline may have an alternative form of bipolar disorder. Available data do not offer strong support for either of these extreme positions and are consistent with a variety of more complex relationships between personality and affective disorders, as outlined elsewhere by Akiskal et al. (60). Personality disorders may simply mimic bipolar disorder, especially when they coexist with substance abuse (see below). They may also contribute to the development of bipolar disorder by unmasking latent symptoms. In addition, character disorders could in some cases result from developmental factors associated with growing up with bipolar disorder itself, with the liability to bipolar disorder, or with affected parents. Last, personality disorders may be modifiers of course, severity, or outcome.

The current division between affective and personality disorders may remain clinically useful in separating what appear to be state phenomena associated with affective episodes from trait phenomena associated with character pathology, but the substantial overlap between these phenomena make it quite problematic. A clearer picture of this complex area must await more family and outcome data on the relation of bipolar disorder to borderline and other personality disorders.

SUBSTANCE ABUSE

Concerns about an association between substance abuse and bipolar disorder are largely related to their frequent co-occurrence in the same individuals. In addition, there are overlapping symptoms related to intoxication and withdrawal of CNS stimulants and depressants and disparate symptoms related to abuse and dependency per se. The boundary is important because substance abuse and dependence are quite common and entail substantial morbidity and mortality. Understanding the relationship could improve treatment of both disorders and might help prevent the poor outcomes associated with comorbidity. In addition, misdiagnosis due to mimicry and masking may mar genetic and other research efforts.

There is substantial evidence for co-occurrence of bipolar disorder and substance abuse. Extensive comor-

bidity has long been reported in both clinical and population studies, including the Epidemiologic Catchment Area study (61). Several studies support the clinical wisdom that drinking is probably concentrated in the manic phase (62, 63). There is little support from family data for any shared etiology, although a recent study (George Winokur, personal communication) may call into question the prevailing wisdom that the greater alcoholism in families of bipolar probands is limited to relatives of *alcoholic* bipolar probands (4, 62, 64).

Bipolar disorder seems to be a risk factor for substance use and abuse, whether as self-medication (63) or simply because of impulsivity during the manic phase, but so far there are few data to support considering alcohol abuse as a variant of bipolar disorder. It is, however, important to be aware that affective syndromes may be difficult to diagnose in substance abusers and that one must consider both false negatives due to masking—especially of hypomania—and false positives due to mimicry, a particular concern with cocaine.

CHILDHOOD SYNDROMES

Critical issues for bipolar disorder's relation to childhood disorders include not only mania and depression of childhood onset but also attention deficit hyperactivity disorder. An understanding of these relationships could contribute to a developmental understanding of bipolar disorder.

It appears clear that adolescent-onset mania—which may be misdiagnosed as schizophrenia due to its more severe and bizarre presentation (65), but shows a long-term course similar to that of bipolar disorder (66)—is part of bipolar disorder. As for the much rarer childhood-onset variant, the relationship is less certain, and adequate follow-up and family data are lacking. Case reports, along with data from studies of children at risk, tend to support a relationship based on course of illness, family relationships, and response to treatment, but sample sizes are far too small to draw a firm conclusion (67–70).

The relation of childhood and adolescent depression to bipolar disorder is still less certain, but the association of earlier age at onset with increased switching from unipolar disorder to bipolar disorder raises a concern (21, 71). Family data are consistent with but not indicative of a relationship, perhaps due to small samples (69, 70, 72). While a larger fraction of childhood (and/or adolescent) than adult depression may be related to bipolar disorder, it would be inappropriate to conclude that childhood depression is a variant of bipolar disorder.

The relation of bipolar disorder to attention deficit hyperactivity disorder is in some ways the most intriguing (the term “attention deficit hyperactivity disorder” is used here, but many studies use *DSM-III* “attention deficit disorder with hyperactivity” or older diagnostic categories). The phenomenology involves overlapping symptoms, including distractibility, hyperactivity, and

impulsivity. Extensive data confirm the co-occurrence of attention deficit hyperactivity disorder with depression, and there are some suggestions for co-occurrence with bipolar disorder as well (73). Follow-up data are less revealing. While there are a number of case reports of a “switch” from attention deficit hyperactivity disorder to bipolar disorder (74, 75), the largest follow-up study (76) did not show increases in affective disorders among 18-year-olds with histories of attention deficit hyperactivity disorder. Family data are interesting but preliminary. There are clear increases in depression among the relatives of children with attention deficit hyperactivity disorder, even if the probands are not depressed (77). The same studies have found specific increases in mania, although none of these was statistically significant. As with depression, data from studies of children at risk have been equivocal, possibly due to sample size considerations (69, 70). It seems fair to conclude that much is suggestive of a possible relation between attention deficit hyperactivity disorder and bipolar disorder, but data are quite sparse. The existing data are consistent with explanations such as mimicry (or misclassification), prodrome, shared etiology, or chance. In any case, the relationship seems unlikely to apply to more than a small fraction of children with attention deficit hyperactivity disorder.

SECONDARY MANIA

The boundary of bipolar disorder and organic affective syndromes hinges on the issue of secondary *mania*, the sine qua non of bipolar disorder. There are several areas of concern, including endocrine, pharmacologic, and structural factors. While the numbers are fairly small, there is always a concern about misdiagnosing cases of secondary mania as bipolar disorder (78). In addition, the issue is important because of its vast potential impact on our understanding of disease process and etiology. Because the area is very broad and the data are fairly limited, the relevant issues can only be touched on.

The possible role of endocrine factors in bipolar disorder is in some ways the most interesting. Because of its strong effects on cognitive, motor, and appetitive functions, bipolar disorder reads as an endocrine disorder. While abnormalities of multiple endocrine systems are frequently reported, they tend to be highly inconsistent (79). A number of provocative observations suggest roles for corticosteroid, thyroid, and reproductive hormones, but despite extensive searches, no explanation for the pathophysiology of mania has emerged from endocrine studies (4).

Most of the pharmacologic agents that mimic or precipitate mania are stimulants and antidepressants, but there are multiple case reports and reports on series of patients regarding other agents as well (4, 80). The role of stimulants and L-dopa has drawn attention because of the interest in biogenic amines and affective disorders (4). The role of antidepressants, discussed above, has

also been related to the biogenic amine hypothesis and raises several clinical and theoretical concerns as well.

Studies of mania related to changes in brain structure have been less revealing (4). Despite multiple reported cases of mania following various head injuries and strokes (81), no consistent localizing findings have emerged, although there is a suggestion of a predominance of right-side lesions (82). However, substantial rates of abnormalities of the ventricles (4, 83) and of subcortical white matter (83, 84) have been reported in bipolar subjects and may represent an as-yet unidentified cause of secondary mania or simply a risk factor for typical bipolar disorder.

DISCUSSION

The many ambiguities in the delineation of bipolar disorder, a well-defined diagnosis supported by a considerable accumulation of data, should serve as a strong warning against any false reassurance proffered by apparently unambiguous *DSM-III-R* criteria. A range of complex and interacting issues contribute to the difficulties with our diagnostic system. We can view these difficulties as resulting from the implementation of the criteria (diagnostic reliability), the criteria themselves (diagnostic validity), the fundamental nosologic process, and aspects of the phenomena themselves.

Interpreting the results of research on diagnostic boundaries leaves us critically dependent on diagnostic reliability precisely where it is most questionable. The more a "boundary" represents a true continuum or overlapping symptoms, the less reliably can patients whose symptoms fall close to the line be diagnosed. Drawing on the example of bipolar disorder and schizophrenia, Kendler (42) demonstrated the perils of misclassification in family studies (where it is a particular problem because of the relatively poor quality of diagnostic evaluations of relatives), but no study of response to treatment, course of illness, or biological markers is immune. Thus, any conclusions about how each of two disorders with overlapping symptoms seems to be only partially responsive to a treatment thought specific for the other, or how an intermediate mean age at onset is observed for a disorder that forms a boundary between two other diagnoses, must be taken with a grain of salt. Such data are often equally compatible with the idea of truly separate disorders that are unreliably distinguished.

A critical issue for diagnostic validity is the choice of validators. A preference for etiologically defined disorders (9, 10) may encourage reliance on family and related studies to validate criteria for bipolar disorder, for which genetic factors are the most identifiable etiologic agents. For other disorders, there may be no reason to favor genetic validators, and we should be open-minded about what will prove the most useful in the long run. Even for bipolar disorder, the knowledge that all validators do not necessarily agree on the best set of criteria (8) should temper the emphasis on genetic validators. For instance, recurrent unipolar disorder ap-

pears to be more lithium-responsive (24), but family studies suggest that patients with three unipolar episodes are *less* likely to have relatives with bipolar disorder than those with a single episode (3). Treatment-response validators are quite problematic for making etiologic diagnoses (9) but may be best when determining criteria for clinical decision making.

Another critical issue is the trade-off between sensitivity and specificity, especially when we are interested in drawing lines between disorders lying along a continuum (e.g., bipolar disorder and cyclothymia) or with overlapping symptoms (e.g., bipolar disorder and schizophrenia). In some settings, it makes sense to maximize specificity and limit ourselves to more severe or more classic forms. In others, it may be more important to maximize sensitivity, and tolerate some individuals whose underlying disorder may be different, in order to capture everyone who is "truly" bipolar. At times, we may even want to cast a net as wide as the very inclusive bipolar spectrum proposed by Akiskal and colleagues (59, 85). Receiver operating characteristic analysis (86), which plots the sensitivity and specificity of a diagnostic test (e.g., a set of criteria) as a function of the cutoff (e.g., in number of symptoms or severity) for a positive result, can be used to compare the available information in different tests or to help tailor the cutoff value to the needs of a given setting.

In *DSM-III-R*, we have chosen a multiaxial system that is categorical rather than scaled and binary rather than probabilistic. The multiaxial system is at its best in distinguishing trait from state, such as personality traits (or disorders) from episodic ailments like bipolar disorder, but, as demonstrated here, it remains quite problematic. The remaining features of the system are modeled on medical nosology. Unfortunately, psychiatry's understanding is far behind its nosologic standards at the present time and may never catch up (9). At least at this stage of our development as a field, scaled or probabilistic alternative systems may offer certain advantages.

A categorical system has innate appeal but makes only limited sense when one is dealing with a true continuum such as mania and hypomania. Scales would facilitate the use of different cutoffs in different settings and would also allow psychiatrists to rate individual patients on separate dimensions (9, 10). For instance, at the boundary of bipolar disorder and schizophrenia, psychosis, chronicity, impairment, and affective symptoms may not sort together, and ratings on each of these dimensions might be more descriptive than labels such as schizophrenia, bipolar disorder, and schizoaffective disorder, bipolar type.

Similarly, a *binary* categorical system, in which the patient either has the disorder in question or does not, also has intuitive appeal, but a probabilistic system might have more utility. Clinicians use unspoken probabilistic systems quite frequently. They may pursue an organic workup more vigorously the less the picture resembles classic bipolar disorder, or prescribe antidepressants more carefully the more a unipolar pa-

tient has bipolar features or bipolar relatives. In research settings, a more formalized probabilistic diagnosis could prove quite useful indeed. For instance, a probability scale for certainty of diagnosis could be based on how thoroughly relatives have been evaluated in a family study or how closely they match the classic form of the diagnosis. Such probability scales have also been proposed as weighting schemes, for instance, weights based on the probability of underlying bipolar disorder among unipolar relatives in a linkage study (87).

Underlying all of these boundary problems is the fact that mental illness may not be a jointed creature, easily divisible into its component parts (8, 9). The substantial comorbidity of bipolar disorder and personality disorders may be an artifact of drawing an artificial line between two parts of an illness with a shared etiology. Another artifact may be our creation of boundary disorders such as bipolar II disorder and schizoaffective disorder. These may benefit research efforts by creating more homogeneous categories. Nonetheless, differences between the boundary disorder and the categories on either side support neither the validity of those adjacent categories nor, in general, the validity of the boundary disorder itself.

CONCLUSIONS

One of the problems with *DSM-III-R* is that it tries to be all things to all people. It is meant to be used for treatment decisions, billing, courtrooms, epidemiologic research, clinical trials, genetic linkage studies, and so on. In reality, each of these settings has different goals and therefore different needs, and the best way to satisfy these needs may be different for different diagnostic groups as well. While a classification system that suits everyone's needs and conforms to the same structure across a broad range of conditions appears to be a laudable goal, it may not be achievable, and its pursuit entails compromises that might, in the long run, cause more problems than they solve.

Under these circumstances, how shall we proceed? We surely cannot discard the gains that formal diagnostic criteria have brought us over the last 20 years. Without the current categorical system, most of the research findings used here to discuss its limitations would not be available. Instead, we must maintain our awareness of these limitations and take steps to overcome them whenever possible. This can best be accomplished by being more flexible in our diagnostic thinking and more innovative in our diagnostic practice. In future versions of the diagnostic manual—if not in *DSM-IV*, then in *DSM-V*—we may wish to consider following the lead of *ICD-10* (88) and coordinating *guidelines* for clinical practice with more explicit *criteria* for research. Beyond this, we may need to develop different sets of criteria for different research purposes, such as clinical trials, linkage studies, and so on. To describe better certain clinical phenomena or to suit particular clinical or research goals, we may need to

abandon simple categorical diagnosis altogether. We have discussed the potential advantages of receiver operating characteristic analysis, scaled or dimensional approaches, and probabilistic diagnosis. Many other options remain to be explored.

At least for bipolar disorder, existing diagnostic criteria may represent the best that can be achieved by using current methods of case definition, but they may not be adequate for a number of research and clinical purposes. As information accumulates on other disorders and diagnostic criteria are refined, similar limits will be reached. If we are to continue our progress toward improved understanding and treatment of bipolar disorder and other psychiatric illnesses, we must begin now to develop the nosologic techniques of the coming century.

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Impact of Psychiatric Hospitalization on Behavioral Complications of Alzheimer's Disease

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Objective: The authors conducted a prospective study of the clinical utility of the four DSM-III-R subtypes of primary degenerative dementia of the Alzheimer type (with delirium, with delusions, with depression, or uncomplicated) and acute psychiatric hospitalization for treatment of these subtypes. **Method:** The subjects were 120 consecutive inpatients with Alzheimer's disease, most of whom had behavioral abnormalities. Each subject received detailed physical, neurological, psychiatric, and mental status examinations. The presence or absence of specific behavioral problems was also documented. Patients were treated with medication, psychotherapy, and behavioral techniques. **Results:** While all patients could be assigned to one of the four DSM-III-R behavioral subtypes, the uncomplicated subtype did not accurately reflect the burden of behavioral symptoms in the patients who did not have delirium, delusions, or depression. Each behavioral subtype responded in a characteristic way to inpatient treatment, as reflected by changes in scores on four psychometric scales used to assess cognitive impairment, psychiatric symptom severity, and level of functioning at admission and at discharge, as well as by changes in residential setting following hospitalization. Half of all patients admitted from their homes and two-thirds of those with depression were able to go home following discharge. **Conclusions:** Behavioral syndromes in Alzheimer's disease should not be overlooked, because they have both clinical and prognostic significance. Short-term psychiatric hospitalization is effective and efficient for achieving the goal of returning patients to their homes and for safely implementing specific treatments in this frail population, and it may reduce the need for institutionalization.

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Primary degenerative dementia of the Alzheimer type (Alzheimer's disease) is characterized by progressive, global cognitive decline. However, aside from

this cardinal feature, there is remarkable individual variability in the age at onset of dementia (1-5), rate of cognitive decline (2, 6-8), presence of extrapyramidal symptoms (2, 9-14), and particular behavioral abnormalities that emerge (14-19). Estimates of the prevalence of behavioral complications in Alzheimer's disease have varied widely depending on the symptom or syndrome of interest, the clinical population studied, and the method used (18). Most estimates of the prevalence of psychosis (delusions or hallucinations) in Alzheimer's disease, obtained from cross-sectional studies of patients in diverse clinical settings, have been in the range of 28%-38% (18). However, longitudinal studies of clinically diagnosed or autopsy-confirmed cases

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of Alzheimer's disease suggest that the prevalence of psychosis may approach 50% by the time of death (14, 17). Similarly, most estimates of the prevalence of depressive disorders in demented outpatients with Alzheimer's disease have been in the range of 10%–25% (18). Both psychosis and major depression confer substantially greater morbidity and worse prognoses upon the demented patients who develop those complications (14, 16, 17). Patients with Alzheimer's disease are also at risk for developing delirium in response to a variety of extrinsic and intrinsic factors (20–22). Like psychosis and major depression, delirium is a potentially reversible condition that may be overlooked in demented patients, markedly reduces functional ability, complicates clinical management, and may terminate in death if the underlying cause is not corrected (20–24).

Unfortunately, there is no known means of preventing Alzheimer's disease, and no effective treatment for ameliorating the symptoms of cognitive impairment or slowing their progression has yet been identified. However, the behavioral symptoms and syndromes that often complicate the treatment of patients with Alzheimer's disease and that typically lead to placements in more highly structured, more expensive, and more restrictive settings are potentially remediable. In controlled studies, neuroleptic drugs have been superior to placebo in reducing the psychotic symptoms of patients with Alzheimer's disease (25). Neuroleptic agents have also been widely used for the nonspecific behavioral management of demented patients, although they may not be more effective in this regard than nonneuroleptic sedatives that lack motor and anticholinergic side effects (25–27). Several reports have suggested that the somatic treatments used to treat major depression in cognitively intact elderly patients—including tricyclic antidepressants (28–30), monoamine oxidase inhibitors (28, 31, 32), and ECT (33)—may also be effective in treating major depression in patients with Alzheimer's disease. Furthermore, controlled studies have supported the use of nonpharmacologic treatments for behavioral symptoms and syndromes in these patients. Finally, educational counseling and the supportive treatment of patients' families can ease the burden of caregiving (34).

Inpatient management of the behavioral complications of Alzheimer's disease provides an opportunity to make a thorough, multidisciplinary diagnostic and functional assessment after the discontinuation of all nonessential medications. In addition to ameliorating drug-induced behavioral abnormalities, this approach also provides a safe means of initiating treatment and carefully titrating doses of psychotropic medication to minimize side effects in this frail population. In our prospective study, we assessed the clinical utility of the four behavioral subtypes of primary degenerative dementia of the Alzheimer type described in *DSM-III-R* (with delirium, with delusions, with depression, and uncomplicated) and their response to short-term psychiatric hospitalization. The investigation was approved by the Institutional Review Board of the University of Pittsburgh.

METHOD

A total of 500 patients with late-life mental disorders were admitted to the geriatric clinical research unit at our hospital from Aug. 31, 1989, to March 15, 1991. A complete history of each patient was taken, and each underwent a physical examination and detailed neurological, psychiatric, and mental status examinations, with laboratory testing and brain imaging as previously described (7, 14, 35, 36). Medical problems were coded according to the *ICD-9-CM* system, with the exception that mental disorders and diseases of the brain were not counted. Psychiatric diagnoses were established according to *DSM-III-R* criteria with the use of information provided by the patient, his or her caregivers and outpatient physicians, and medical records to augment the results of the diagnostic evaluation performed on the unit. The diagnostic criteria of *DSM-III-R* were applied at a consensus conference attended by faculty psychiatrists (including each patient's attending psychiatrist), one of whom was also board-certified in internal medicine, and by research staff members, all with specialized expertise in geriatric psychiatry. Consensus opinions based on all available clinical, historical, and laboratory data were used to differentiate symptoms related to psychiatric syndromes from those attributable to concurrent primary medical illnesses. Of the 500 patients, 120 met the *DSM-III-R* criteria for primary degenerative dementia of the Alzheimer type and were included in the current study. These 120 patients would also meet the criteria of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association for possible or probable Alzheimer's disease (37). The clinical diagnoses of Alzheimer's disease made at our center with the use of similar criteria have been confirmed in approximately 85% of cases that have been autopsied (38).

The patient's behavioral subtype of primary degenerative dementia of the Alzheimer type described in *DSM-III-R*, the presence of other specific behavioral problems, and the age at first onset of dementia were also discussed at the consensus conference and recorded. For the diagnosis of the subtypes with delirium and with depression, the *DSM-III-R* criteria for delirium and major depression were used. The use of the criteria for major depression in the context of primary dementia has been validated by both neuropathological and neurochemical studies of post-mortem brain tissue (16, 39). Delusions were defined as described in *DSM-III-R*. Confabulations and misidentifications were not considered delusions unless they persisted in the face of incontrovertible evidence to the contrary. The patients who did not fulfill the criteria for any of these three subtypes were described as having the uncomplicated subtype, since no other category for primary degenerative dementia of the Alzheimer type exists in *DSM-III-R*.

We also documented the presence or absence of a group of specific behavioral problems, including hallucinations, irritability, aggression, restlessness, wander-

ing, abnormal verbalization, and any other behavioral problem during hospitalization that was judged to compromise significantly a patient's ability to care for himself or herself or to be cared for by others. These behavioral problems were recorded with a checklist that was completed for all patients with dementia. Like delusions, hallucinations were defined as described in *DSM-III-R*. Irritability was defined as a dysphoric state, often experienced subjectively as anger, during which there was an inappropriate threshold for the perception of stimuli as unpleasant or intrusive. Aggression was defined as the threat or commission of physical violence directed toward others or the intentional destruction of property. Restlessness was characterized as an abnormally increased level of motor activity. Wandering was defined as purposeless ambulation, often into socially inappropriate or potentially dangerous places. Abnormal vocalization was characterized as repetitive, stereotypical, or overly loud utterances that were socially inappropriate or disruptive to others. The consensus group also had the opportunity to record any additional behavioral abnormalities that substantially complicated the clinical presentation but were not captured by any of the other behavioral descriptors. Incontinence was not characterized as a behavioral abnormality because it often had multiple causes (e.g., medications, physical disability, infection), rather than being attributable to dementia itself, and because it could not be assessed in patients with urinary catheters. Best estimates of onset of symptoms were reached from historical information provided by the patients, family members, caregivers, and all other available ancillary sources.

The severity of cognitive impairment and behavioral symptoms was rated from information obtained during the first and last 72 hours of hospitalization. This information was reflected by four psychometric scales administered by one to three trained raters who were not involved in the clinical management of the patients. The Mini-Mental State examination, an 11-item series of interviewer-administered cognitive tasks (0=worst score, 30=best score) was used because it provides a reliable and valid index of cognitive impairment in the elderly (40). The severity of depressive symptoms was assessed with the 17-item Hamilton Rating Scale for Depression (41), which has scores ranging from 0 (best) to 52 (worst). While there is some overlap in the symptoms scored by the Hamilton depression scale and the Brief Psychiatric Rating Scale (BPRS) (42), the BPRS was also used because it is sensitive to the severity of psychotic symptoms. Scores on the BPRS range from 18 (best) to 126 (worst). Both the Hamilton depression scale and the BPRS were completed by using information from direct observation or from the medical record during the time intervals described. Finally, the Global Assessment Scale (GAS) (43) was used to assess overall level of functioning; scores range from 1 (worst) to 100 (best). This scale is rated using anchor points with brief clinical descriptions at 10-point increments. An estimate of the risk for cerebrovascular disease was made with the ischemic score of Hachinski et al. (44), as

modified by Rosen et al. (45). The interrater reliability of these instruments was reflected by intraclass correlation coefficients of 0.78 or greater.

The physical environment of the inpatient unit was designed to facilitate the care of frail elderly patients, and relatively standardized approaches have been developed for managing dementia and its behavioral complications. Initial attention was focused on the formulation of a comprehensive diagnosis and on minimizing the burden of medical problems that often contribute to functional impairment. Causes of delirium were aggressively sought and appropriate interventions made while supportive care was provided.

Medications were the most common cause of delirium in our clinical setting, although it was often impossible to identify a single cause from among multiple contributing factors. Psychosis (delusions or hallucinations) was treated with high-potency neuroleptics, typically haloperidol, 1–4 mg/day, or perphenazine, 8–24 mg/day. In our experience, higher doses frequently lead to increased confusion from the anticholinergic effects of the medications (25, 46) or to debilitating extrapyramidal side effects, especially parkinsonism (25). Low-potency neuroleptic agents are not well tolerated in equivalent antipsychotic doses because of anticholinergic side effects and symptomatic hypotension.

We have successfully and safely used a variety of antidepressant medications and ECT for the treatment of major depression in patients with Alzheimer's disease. However, our initial treatment of choice for this behavioral complication is nortriptyline, because of the availability of testing of blood levels, which facilitates the adjustment of oral dosages (47), the favorable profile of the drug's side effects (28), and its efficacy in the treatment of major depression in the elderly (28, 29). Therapeutic blood levels (50–150 ng/ml; target=100 ng/ml) (47) are usually reached with doses between 25 and 75 mg/day (28, 29). In the initial stages of the treatment of the patients with Alzheimer's disease and psychosis or depression, antipsychotic or antidepressant medications were often augmented by adjunctive treatment with low doses of short-acting benzodiazepines for symptomatic relief, which were tapered as the behavioral syndromes remitted.

The pharmacologic treatment of behavioral symptoms that occurred in the absence of delirium, psychosis, or major depression was largely empirical and aimed at ameliorating maladaptive behavioral symptoms while producing minimal side effects and without compromising functional ability. Low-dose, high-potency neuroleptic agents, antidepressants, short-acting benzodiazepines, lithium, and carbamazepine were used for this purpose, depending on the behavioral features of the patients and their clinical histories.

In addition to these somatic therapies, patients were provided with supportive individual and group psychotherapy as appropriate. Behavioral techniques were also used, especially for patients whose cognitive impairment limited their ability to benefit from psychotherapy. Finally, education, counseling, and supportive

TABLE 1. Clinical Features of 120 Patients With the *DSM-III-R* Behavioral Subtypes of Primary Degenerative Dementia of the Alzheimer Type^a

Behavioral Subtype	N	%	Age at Admission (years)		Age at Onset (years)		Sex Ratio (M/F) ^b	Race (White/Black) ^c	Mini-Mental State Score at Admission ^d		Modified Ischemic Score ^e		Number of Medical Problems ^f		Length of Hospitalization (days)	
			Mean	SD	Mean	SD			Mean	SD	Mean	SD	Mean	SD	Mean	SD
With delirium	15	13	78.7	7.9	71.1	16.0	9/6	15/0	10.4	5.6	3.7	2.0	5.3	2.6	35.7	13.0
With delusions	49	41	78.8	8.0	74.1	11.5	15/34	40/9	12.8	7.1	2.7	1.6	4.1	2.5	28.2	7.0
With depression	37	31	80.5	7.9	74.4	15.4	9/28	36/1	15.8	5.7	3.4	1.8	5.7	3.0	31.0	7.0
Uncomplicated	40	33	79.3	8.0	74.9	9.1	19/21	40/0	12.5	7.5	2.5	1.6	3.8	2.1	25.7	5.0
All	120	100	79.6	7.5	74.9	10.8	45/75	110/10	13.1	7.1	2.9	1.7	4.4	2.6	27.1	15.7

^aComplete data sets are presented for all variables except the Mini-Mental State examination, which is a performance test requiring patient participation. The numbers of patients in the four behavioral subtypes add to more than 120 because 18 (15%) of the patients met the criteria for more than one subtype.

^b $\chi^2=8.72$, $df=3$, $p=0.03$; pairwise comparisons with $p<0.05$: delirium versus delusions, delirium versus depression.

^cFisher's exact test, $p=0.003$; pairwise comparisons with $p<0.05$: delusions versus depression, delusions versus uncomplicated.

^d $N=11$ for the group with delirium, $N=37$ for the group with delusions, $N=30$ for the group with depression, $N=34$ for the group with uncomplicated Alzheimer's disease, $N=98$ for all subtypes. $F=2.31$, $df=3$, 108 , $p=0.08$.

^e $F=3.14$, $df=3$, 137 , $p=0.03$; no pairwise comparisons with $p<0.05$.

^f $F=4.55$, $df=3$, 137 , $p=0.005$; pairwise comparisons with $p<0.05$: depression versus delusions, depression versus uncomplicated.

psychotherapy were provided to family members and caregivers.

Comparisons of continuous sociodemographic and clinical variables among the patients with the different behavioral subtypes of dementia of the Alzheimer type were made using one-way analyses of variance, followed by Tukey post hoc tests when significant group effects were detected. Eighteen of the 120 patients met the diagnostic criteria for more than one behavioral subtype. Comparisons of discrete variables were made with the chi-square test or Fisher's exact test as appropriate. Comparisons of rating scale scores obtained at admission and at discharge were made with the use of paired *t* tests. Associations between continuous variables were explored using the Pearson correlation coefficient. All statistical tests were two-tailed.

RESULTS

As shown in table 1, the group of demented patients studied had a mean age of 79.6 years, and the mean age at onset of cognitive decline was 74.9 years. The group included 75 women (63%), and 10 (8%) of the subjects were black. Eighty (67%) of the patients were living at home prior to admission, while the remainder were living in personal care or nursing homes. The majority of the patients were living on retirement incomes; the mean annual income was \$11,545 (SD=\$6,105). Fifty-nine (49%) of the patients were high school graduates, 16 (13%) had earned a college degree, and three (3%) had earned a postgraduate degree.

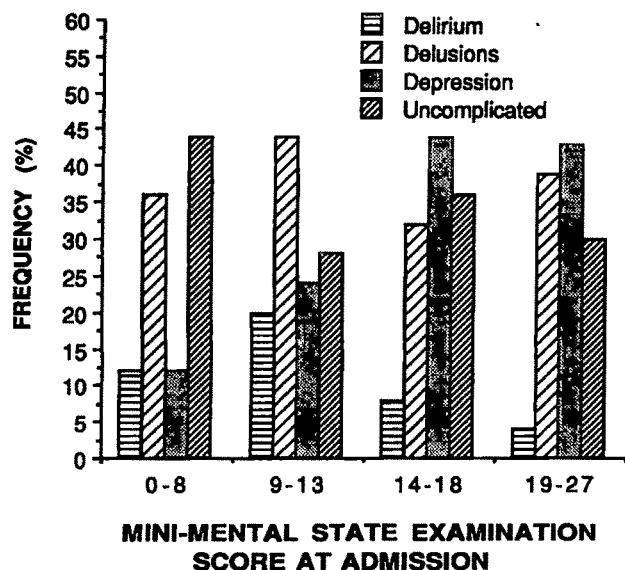
The clinical features of these 120 patients are presented in table 1. The Mini-Mental State examination scores for the 98 patients (82%) who were able to participate in this test of cognitive performance ranged from 0 to 27, with a mean of 13.1. The mean modified ischemic score was 2.9, supporting the diagnosis of primary degenerative dementia of the Alzheimer type rather than dementia of vascular origin. The average

number of medical problems per patient was 4.4, and the average length of hospitalization was 27.1 days.

The distribution of *DSM-III-R* behavioral subtypes is also shown in table 1. Only 18 (15%) of the 120 patients met the criteria for more than one category. Since delirium, delusions, and depression occurred alone in 8%, 26%, and 18% of the patients, respectively, 8.5% ($[0.08 \times 0.26] + [0.08 \times 0.18] + [0.26 \times 0.18] + [0.08 \times 0.26 \times 0.18] = 0.085$) would have been expected to exhibit more than one of these subtypes concurrently, a value that did not differ significantly from the observed 15% ($\chi^2=1.92$, $df=1$, $p=0.17$). Twelve of these 18 patients had major depression and delusions, three had delirium and delusions, and three had delirium, delusions, and depression. As shown in table 1, the behavioral subtypes did not differ significantly in age at onset of dementia, age at admission, level of cognitive impairment at admission, or length of hospitalization. Moreover, the proportion of patients able to participate in the Mini-Mental State examination did not differ among the behavioral subtypes ($\chi^2=1.62$, $df=3$, $p=0.65$). In contrast, significant differences in sex, race, ischemic score, and number of medical problems were observed among the behavioral subtypes. Delirium occurred more commonly in men, while delusions and depression were more common in women. In the group with the uncomplicated subtype, the sex ratio was approximately 1:1. Delusions were more common in black patients than in white patients. In fact, nine of the 10 black patients were delusional. Finally, patients with delirium or depression tended to have higher ischemic scores and more medical problems than patients with delusions or the uncomplicated subtype.

We divided the patients into quartiles according to their Mini-Mental State scores at admission, and the frequency distribution of behavioral subtypes across the resulting quartiles is shown in figure 1. The frequency of the subtype with depression decreased with decreasing Mini-Mental State scores, consistent with a previous report (48). None of the other three *DSM-III-R*

FIGURE 1. Percentages of Patients, Grouped According to Their Mini-Mental State Examination Scores at Hospital Admission, Who Met Clinical Criteria for the *DSM-III-R* Behavioral Subtypes of Primary Degenerative Dementia of the Alzheimer Type^a



^aThe quartile with the highest Mini-Mental State scores contained 23 patients, and each of the remaining quartiles contained 25 patients.

behavioral subtypes showed a consistent relation with Mini-Mental State scores. In contrast, the number of other significant behavioral problems increased with decreasing Mini-Mental State scores ($r=-0.45$, $df=96$, $p<0.001$).

The profile of significant behavioral problems found among the 40 patients with the uncomplicated subtype of Alzheimer's disease is presented in table 2. Patients in this group suffered from a mean of 3.0 (SD=1.7) significant behavioral problems, and only two (5%) had no significant behavioral problems during hospitalization. These two patients were admitted for the diagnostic evaluation of newly identified cognitive decline, suspiciousness, and decreased functional capacity that they evidenced in their residential settings. A comparison of the frequencies of significant behavioral problems in the patients with the uncomplicated and with the other behavioral subtypes is also presented in table 2. Interestingly, with the exception of hallucinations and unspecified problems, the rank order and frequency of each specific behavioral problem were similar in the group with the uncomplicated subtype and the combined group of patients with delirium, delusions, or depression. These findings suggest that the behavioral problems listed in table 2 play an important role in the referral of patients with Alzheimer's disease for inpatient psychiatric treatment and further illustrate the burden of behavioral complications presented by these patients. There was a nonrandom association of hallucinations and delusions ($\chi^2=12.53$, $df=1$, $p<0.001$), supporting the diagnostic validity of psychosis in the context of Alzheimer's disease.

TABLE 2. Significant Behavioral Problems in 120 Patients With the Uncomplicated and Other *DSM-III-R* Behavioral Subtypes of Primary Degenerative Dementia of the Alzheimer Type

Problem ^a	Uncomplicated Subtype (N=40)		Other Behavioral Subtypes ^b (N=80)		Analysis	
	N	%	N	%	χ^2 (df=1)	p
Irritability	31	78	67	84	0.70	0.40
Restlessness	24	60	57	71	1.54	0.22
Aggression	22	55	37	46	0.82	0.37
Wandering	21	53	28	35	3.38	0.07
Verbalization	9	23	18	23	0.00	1.00
Hallucinations	4	10	27	34	7.85	0.005
Unspecified	7	18	2	3	8.65	0.003
None	2	5	6	8	0.27	0.61

^aSignificant unspecified behavioral problems included public masturbation or defecation, other significant sexual or social disinhibition, debilitating sleep disturbance, hoarding behavior, and food refusal leading to malnutrition.

^bWith delirium, with delusions, and with depression.

Response to treatment, as reflected by changes in scores on the four psychometric scales, is presented in table 3. The patients with delirium exhibited greater improvement in cognitive performance than the patients with any other behavioral subtype, as reflected by an average change in Mini-Mental State score of more than 4 points. Patients with delirium also exhibited significant improvement in their Hamilton depression scale scores; however, this finding is difficult to interpret in light of the small size of this group and the fact that three of these patients also met criteria for primary degenerative dementia of the Alzheimer type with depression. In spite of their cognitive improvement, patients with delirium did not exhibit significant improvement on the BPRS, and no significant improvement in functioning was observed. Forty-five (92%) of the 49 patients with delusions received neuroleptic medications, and all 37 patients with depression received treatment with an antidepressant, lithium, or ECT. Thirty-two (87%) of the latter group received treatment with nortriptyline. The patients with delusions or depression demonstrated significant improvement on all four scales, with the greatest symptomatic improvement reflected by changes in the BPRS and Hamilton depression scale scores, respectively. The response of the depressed patients was the most vigorous of the four subgroups, as reflected by a 7.0-point average reduction in the Hamilton depression score and a 9.1 average increase in the GAS score, even though this subgroup experienced the greatest number of medical problems (table 1). The patients with the uncomplicated subtype who had mixed behavioral symptoms were the only subtype not to experience consistent, albeit modest, cognitive improvement. However, they did manifest an improvement in the severity of their behavioral problems, as reflected by the Hamilton depression and BPRS scores, and an improvement in overall level of functioning, as reflected by the GAS score.

A comparison of residential setting before admission

TABLE 3. Response to Inpatient Treatment of 120 Patients With the *DSM-III-R* Behavioral Subtypes of Primary Degenerative Dementia of the Alzheimer Type^a

Behavioral Subtype/Measure	At Admission		At Discharge		Change Between Admission and Discharge		Analysis			Paired Observations	
	Mean	SD	Mean	SD	Mean	SD	t	df	p	N	%
With delirium											
Mini-Mental State score	12.0	5.9	16.3	7.5	4.3	3.2	3.34	6	0.01	7	46.7
Hamilton depression score	19.5	4.6	12.8	3.3	-6.7	3.1	-5.31	5	0.003	6	40.0
BPRS ^b score	38.1	4.5	34.9	4.6	-3.3	7.3	-1.20	6	0.28	7	46.7
GAS ^c score	23.3	7.8	24.5	9.4	1.2	4.3	1.02	12	0.33	13	86.7
With delusions											
Mini-Mental State score	12.8	7.0	14.3	7.0	1.3	0.6	2.61	32	0.05	33	67.3
Hamilton depression score	16.5	4.8	13.1	4.4	-3.4	4.3	-4.28	28	<0.001	29	59.2
BPRS ^b score	40.0	6.3	34.8	5.7	-5.1	5.9	4.78	29	<0.001	30	61.2
GAS ^c score	24.8	7.5	30.4	12.0	5.6	8.9	4.31	45	<0.001	46	93.9
With depression											
Mini-Mental State score	16.4	5.9	18.5	4.1	2.1	4.0	2.58	23	0.02	24	64.9
Hamilton depression score	20.7	4.7	13.7	3.2	-7.0	3.9	-8.89	23	<0.001	24	64.9
BPRS ^b score	36.8	5.9	32.3	4.9	-4.5	5.5	-4.07	24	<0.001	25	67.6
GAS ^c score	29.3	8.5	38.3	12.4	9.1	9.9	5.28	32	<0.001	33	89.2
Uncomplicated											
Mini-Mental State score	13.0	7.3	12.8	7.9	-0.2	3.4	-0.33	27	0.73	28	70.0
Hamilton depression score	13.3	4.0	11.4	4.1	-1.8	3.6	-2.53	24	0.02	25	62.5
BPRS ^b score	33.6	4.9	30.4	5.4	-3.2	2.6	-6.29	25	<0.001	26	65.0
GAS ^c score	25.3	9.1	30.0	12.8	4.7	6.5	4.36	36	<0.001	37	92.5

^aPatients who did not have assessment scores at admission and discharge were omitted.^bBPRS=Brief Psychiatric Rating Scale.^cGAS=Global Assessment Scale.

with that following discharge is presented in table 4. The proportion of patients who had been living at home was consistent across the behavioral subtypes, ranging from 60.1% to 65.3%. The remaining patients were admitted to the hospital from either personal care or nursing homes. Consistent with the clinical course of Alzheimer's disease and the fact that the typical reason for referral to inpatient care was the inability to manage the patient safely in his or her residential setting, a significant fraction of patients required transfer to a more restrictive setting following discharge. This pattern was consistent across all of the behavioral subtypes except depression, reflecting the greatest symptomatic and functional improvement of this subtype during hospitalization (table 3). In spite of the general trend, 43 (53.8%) of the 80 patients who could no longer be managed at home prior to admission were able to return home following discharge. Moreover, this proportion reached 66.7% (16 of 24) among the subtype with depression. Finally, one patient who had been admitted to a personal care home when he developed restlessness and wandering behavior was able to return home following discharge.

DISCUSSION

Behavioral abnormalities are a common and important source of morbidity and mortality among patients with Alzheimer's disease. However, the diagnosis and treatment of behavioral syndromes and symptoms in

TABLE 4. Residential Setting Before Admission and Discharge Disposition of 120 Patients With the *DSM-III-R* Behavioral Subtypes of Primary Degenerative Dementia of the Alzheimer Type

Behavioral Subtype	Home		Personal Care or Nursing Home		Long-Term Hospital	
	N	%	N	%	N	%
With delirium (N=15)						
Admission	9	60.1	6	40.0	0	0.0
Discharge	4	26.7	7	46.7	4	26.7 ^a
With delusions (N=49)						
Admission	32	65.3	17	34.7	0	0.0
Discharge	18	36.8	24	48.9	7	14.3 ^b
With depression (N=37)						
Admission	24	64.9	13	35.1	0	0.0
Discharge	16	43.2	19	51.3	2	5.4
Uncomplicated (N=40)						
Admission	26	65.0	14	35.0	0	0.0
Discharge	11	27.5	25	62.5	4	10.0 ^c
All (N=120)						
Admission	80	66.7	40	33.3	0	0.0
Discharge	43	35.8	63	52.5	14	11.7 ^d

^aSignificantly different from admission value ($\chi^2=6.00$, $df=2$, $p=0.05$).^bSignificantly different from admission value ($\chi^2=7.60$, $df=2$, $p=0.02$).^cSignificantly different from admission value ($\chi^2=13.18$, $df=2$, $p=0.001$).^dSignificantly different from admission value ($\chi^2=30.27$, $df=2$, $p<0.001$).

demented patients remain in the formative stages. Our prospective study provided an empirical assessment of diagnostic criteria for the behavioral subtypes of pri-

mary degenerative dementia of the Alzheimer type described in *DSM-III-R*, as well as a quantitative evaluation of response to targeted inpatient treatments based on the resulting diagnoses. Although the patients in our study exhibited a wide range of cognitive impairments, it was possible to reach a consensus on the assignment of each of the 120 patients to one of the four behavioral subtypes by using the criteria described in *DSM-III-R*. The subtypes with delirium, delusions, and depression appeared to occur independently, since only 15% of the patients met the criteria for more than one of these subtypes concurrently. Furthermore, the patients with each behavioral subtype responded to inpatient treatment in a characteristic way, as revealed by changes in scores on the psychometric scales used to assess cognitive impairment, psychiatric symptom severity, and level of functioning. The therapeutic response we observed seemed to be clinically significant as well as statistically significant. While the patients had typically been hospitalized because they could no longer be safely managed at home, half of all patients who had been living at home prior to admission and two-thirds of those with major depression returned home following discharge. In light of the progressive deterioration that is characteristic of Alzheimer's disease, the short-term inpatient psychiatric care provided appears to have been successful.

It should be emphasized that the goal of short-term inpatient treatment was the completion of a thorough diagnostic assessment and the initiation of a comprehensive treatment plan. Discharge occurred when therapeutic doses of medications were achieved and the patient was judged to be sufficiently stable that a safe disposition could be effected with appropriate aftercare. Therefore, our assessments probably underestimated the effects of the treatments initiated, because the maximal benefits of antidepressant and neuroleptic therapy occur 1–2 months after the establishment of optimal doses (28, 49). The interpretation of our quantitative assessments of response to inpatient treatment is also limited by the exclusion of patients who were unable to participate in the assessments at admission or discharge. Unfortunately, this methodologic limitation is inherent in the study of moderately to severely demented patients, especially those who have significant behavioral problems. We addressed this issue by including an analysis of changes in residential setting, which was in general agreement with the psychometric data. It should also be emphasized that our study was naturalistic in its design and was intended to provide an assessment of the aggregate of somatic and other treatment modalities that constitute geriatric inpatient care in our tertiary care setting. The relative contributions of the individual interventions cannot be determined from our data.

Two suggestions for revision of the *DSM-III-R* behavioral subtypes of primary degenerative dementia of the Alzheimer type seem warranted. The use of the uncomplicated subtype to describe psychiatric inpatients with Alzheimer's disease who do not suffer from delirium, delusions, or depression is inaccurate and often

offends family members and other caregivers who have been making their best attempts to manage disruptive and potentially dangerous behavioral abnormalities. Furthermore, the use of this misnomer may jeopardize third-party reimbursement for inpatient treatment in circumstances where it may be clearly indicated. For these reasons, we favor the addition of an additional behavioral subtype for primary degenerative dementia of the Alzheimer type to denote the presence of one or more other significant behavioral abnormalities.

We also favor replacement of the delusional subtype with a psychosis subtype that would include either delusions or hallucinations, since these psychotic symptoms assorted nonrandomly in our inpatient population as well as in a previous longitudinal study of outpatients with Alzheimer's disease (14). As described in *DSM-III-R*, these symptoms constitute direct evidence of psychosis. We do not endorse the use of a broader definition of psychosis because disorganized or aberrant behavior in the context of dementia is often attributable to cognitive impairment rather than a disturbance of reality testing. This definition of psychosis in the context of primary degenerative dementia of the Alzheimer type has also been validated by longitudinal studies that have found the presence of psychosis to be associated with a more rapid rate of cognitive decline (14, 17) and by post-mortem studies that have revealed neuropathological and neurochemical correlates which appear to be relatively specific for psychosis (19). We did not present the data on response to treatment separately for the patients who met criteria for psychosis because this group largely overlapped with the delusional subtype and because the addition of the patients who had hallucinations without delusions did not significantly change the results.

In summary, the diagnosis of behavioral syndromes and symptoms that commonly emerge in primary degenerative dementia of the Alzheimer type is a feasible goal that should not be overlooked, because it has both clinical and prognostic significance. Short-term psychiatric hospitalization provides an effective and efficient means for achieving this goal and for safely implementing treatments that are targeted to specific behavioral complications in this frail population. It may also reduce the need for institutionalization.

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Psychiatric Outpatient Practice: Patterns and Policies

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***Objective:** The purpose of this paper is to explore possible consequences of recent changes in the Medicare payment schedule for office-based psychiatric services. **Method:** Psychiatric office visits from the 1985 National Ambulatory Medical Care Survey were categorized in a manner that approximates commonly used codes of the Physicians' Current Procedural Terminology. An analysis was conducted of the frequency and clinical characteristics of various types of services, focusing particularly on visits of under 20 minutes in length that included a medication prescription (medication visits) and other visits of 35 minutes or less in duration (brief visits). **Results:** Medication visits and brief visits together accounted for more than one-quarter (27.3%) of all U.S. psychiatric office visits. The relative risk of receiving these short visits was greater for patients who paid with public resources, were over 65 years of age, were nonwhite in race (brief visits only), received a prescription for an antipsychotic medication, or were diagnosed as having a psychotic disorder. **Conclusions:** Short office visits are provided to a particularly vulnerable patient population. The reduction in Medicare copayments for medication management services should increase the patient demand for these short visits. However, where the new Medicare schedule has lowered physician fees for these services, the financial incentive to provide short visits will decrease and patient access may become limited.*

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Psychiatrists in private practice continually grapple with the conflict between a desire to provide comprehensive care and the drive to use time in an efficient manner. The length of time psychiatrists actually spend with individual patients is influenced by a variety of factors. Patient age is inversely related and illness severity is directly related to the amount of face-to-face treatment that patients receive each month (1). Psychiatrists who are influenced by psychoanalytic treatment, practice in medical school settings, or practice in areas that are receptive to mental health services tend to provide comparatively more time-intensive care (1).

Psychiatrists have historically priced brief office visits proportionately higher than standard psychotherapy visits (2). In 1991, the median fee (\$61.00) for a 20- to 30-minute psychotherapy session (code 90843 in the *Physicians' Current Procedural Terminology* [CPT] [3]) was substantially more than half the median fee for a 45- to 50-minute psychotherapy session (\$93.00, CPT code 90844) (4). This pricing strategy has impor-

tant financial consequences. One of the reasons male psychiatrists earn more than female psychiatrists is that male psychiatrists see more patients per hour than their female counterparts (5).

Of the various mental health professions, psychiatry is the most heavily dependent on third-party payment. Although Medicare pays for only a small proportion of outpatient psychiatric care (6), Medicare policies frequently serve as a bellwether for other third-party payers (7). For this reason, mental health policy analysts pay particular attention to the design of Medicare policies.

In December 1987, Medicare expanded its coverage of outpatient psychiatric services provided during "medical management" visits (8). Patient copayment was lowered from 50% to 20% and dollar limits were eliminated. The 50% patient copayment was maintained for all other outpatient psychiatric services. Medicare policy is based on a narrow definition of "medical management," usually brief office visits related to evaluating, prescribing, and monitoring psychoactive medication. This activity typically is given the CPT code for "medication management" (code 90862), although practitioners in some jurisdictions have worked out additional codes. More broadly defined, "medical management" refers to a variety of office visits during which psychotherapy is *not* the dominant activity. Almost any clinical encounter other than a psychotherapy session might be considered in this category. In

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theory, the "evaluation and management" codes for office visits could be used for medical management. Practice varies from location to location, and there continue to be problems in implementing this concept and the changes in reimbursement it represents.

In January 1992, Medicare began to phase in a new physician fee schedule to control medical expenditures. The new schedule, which is derived from a resource-based relative values scale (RBRVS), arrived at physician fees by analyzing actual practice costs rather than customary or historical charges (9-11). In several areas, the RBRVS schedule substantially reduced physician fees for the less time-consuming outpatient psychiatric services. Psychiatrists in New York City, for example, experienced a 35% reduction in their Medicare fee for 20- to 30-minute medical psychotherapy sessions (CPT code 90843) and a 42% reduction in their fee for medication management visits (CPT code 90862). The reductions for longer outpatient psychiatric services tended to be more modest. For psychiatrists in New York City, there was a 7% reduction in the fee for 45- to 50-minute individual psychotherapy sessions (CPT code 90844) and a 12% reduction for psychiatric diagnostic interviews (CPT code 90801) (12).

The impact of the RBRVS Medicare Fee Schedule varies from location to location. Fees in New York City were adversely affected by the adjustments made for geographic region, which favored rural areas over metropolitan centers. Not every location will experience the same reductions; some will experience an increase in fees, especially for certain categories of visits. In some locations certain services were historically undervalued; in others certain services were overvalued. Although fees for psychiatric outpatient practice will remain about the same in the aggregate, specific adjustments in fees and changing reimbursement policies will alter the incentives shaping supply and demand for ambulatory psychiatric services throughout the nation.

In the current paper, we evaluate how these changes in reimbursement policy may influence office-based psychiatric practice. Data are drawn from the 1985 National Ambulatory Medical Care Survey, and visits are classified to approximate CPT codes commonly used in office practice: psychiatric diagnostic interview (code 90801), medication management (code 90862), individual medical psychotherapy of approximately 20 to 30 minutes (code 90843), and individual medical psychotherapy of approximately 45 to 50 minutes (code 90844). For heuristic reasons, we also analyze visits that are greater than 55 minutes in length.

METHOD

Source of Data

The National Ambulatory Medical Care Survey samples a nationally representative group of visits to physicians in office-based practice. Patient visits are sampled by a one-page data form that was completed by the at-

tending physicians or their office staff. This form contains items such as the patient's age, sex, diagnoses, medications prescribed, and duration of the visit.

The National Ambulatory Medical Care Survey uses a multistage probability sampling design. This involves sampling primary sampling units, sampling physician practices within these units, and sampling patient visits among these physician practices. To reduce duplication of individuals, each sampled physician is randomly assigned to participate during one of the 52 weeks in the survey year. A systematic random sample of visits is selected by the physician during the assigned week. Although this strategy oversamples frequent users of office-based medical care, it accurately reflects clinical activity.

A weighting system was developed by the National Center for Health Statistics to produce national estimates from sample estimates (13). National estimates are obtained by summing the "patient weights." The construction of the patient weights has the following three components: 1) inflation by the reciprocal of the sampling probability, 2) adjustment for nonresponse, and 3) a ratio adjustment to fixed totals. The adjustment for nonresponse replaces patient visits to nonrespondent physicians with visits to respondent physicians in the same specialty and primary sampling unit. The ratio adjustment involves multiplying each visit by the ratio of physicians listed in the master files of the American Medical Association-American Osteopathic Association

Visit Sample

Analyses are presented of visits to physicians who listed their specialty as psychiatry. Psychiatrists include physicians specializing in general psychiatry, child psychiatry, psychoanalysis, and other psychiatric subspecialties. The 1985 National Ambulatory Medical Care Survey surveyed 178 psychiatrists, and the response rate was 74%. A total of 2,703 psychiatric visits were sampled.

Visit Categories

Several of the analyses involve aggregating the psychiatric visits into five mutually exclusive categories. These categories include 1) diagnostic interviews, 2) medication visits, 3) brief visits, 4) standard visits, and 5) extended visits.

Diagnostic interviews include all visits by patients who have not been previously seen by the surveyed psychiatrist and all visits for new psychiatric conditions. Medication visits include all visits of under 20 minutes that include the prescription of a medication. Brief visits include all visits of between 20 and 35 minutes and all visits of less than 20 minutes that do not include a medication prescription. Standard visits include all visits that are greater than 35 minutes and less than 56 minutes in duration. Extended visits include all visits that are greater than 55 minutes.

TABLE 1. Distribution of Office Visits to Psychiatrists Among Solo, Group, and Other Practices^a

Visit Category	Percent		
	Solo Practice	Group Practice	Other
Diagnostic interviews	7.3	15.1 ^b	8.2 ^c
Medication visits	6.0	9.4 ^d	7.1 ^c
Brief visits	15.7	38.4 ^b	24.7 ^e
Standard visits	61.0 ^f	28.7	50.4
Extended visits	10.0	8.3	9.5 ^c

^aData from 1985 National Ambulatory Medical Care Survey (13) based on 2,703 psychiatric visits. Percents based on weighted sampling.

^bSignificantly different from solo practice ($p < 0.001$).

^cEstimate with relative standard error that exceeds 40%.

^dSignificantly different from solo practice ($p < 0.01$).

^eSignificantly different from solo practice ($p < 0.05$).

^fSignificantly different from group practice ($p < 0.001$).

Diagnostic Groups

The National Ambulatory Medical Care Survey records diagnoses according to ICD-9-CM. In the current report, specific diagnostic codes have been aggregated into seven broad diagnostic groups. These groups include psychotic disorders (codes 290–295, 296.0, 296.1, 296.4–299), depressive disorders (codes 296.2, 296.3, 300.4, 311), neurotic disorders (codes 300.0–300.3, 300.5–300.9), personality disorders (code 301), adjustment disorders (code 309), substance abuse related disorders (codes 291–292, 303–305, 327–328), and a residual category of all other disorders and conditions.

Statistical Methods

The percentages and means provided in the current report are based on weighted estimates. The National Center for Health Statistics provides tables for calculating the approximate standard errors of the survey estimates (13). These tables were used to compute *t* test statistics, and comparisons were made for statistical significance with the two-tailed *t* test and infinite degrees of freedom. Tests of statistical significance are not performed with survey estimates that have an associated relative standard error which exceeds 40%.

Logistic regressions were used to compute the odds ratios of brief visits and medication visits for selected independent variables. The regressions were computed with unweighted data.

RESULTS

General

In 1985, U.S. office-based psychiatrists provided approximately 18 million patient visits. Standard visits accounted for a majority of these contacts (54.3%). Brief visits (20.6%), extended visits (9.7%), diagnostic interviews (8.8%), and medication visits (6.7%) accounted for proportionately fewer visits.

TABLE 2. Geographic Distribution of Office Visits to Psychiatrists^a

Visit Category	Percent			
	Northeast	Midwest	South	West
Diagnostic interviews	6.3	14.4 ^b	8.6	7.3
Medication visits	6.4	8.4 ^c	7.3	4.8
Brief visits	14.9	21.0	29.0 ^d	21.3
Standard visits	65.9 ^e	43.3	44.1	56.5
Extended visits	6.5	13.0 ^d	11.0 ^d	10.1 ^d

^aData from 1985 National Ambulatory Medical Care Survey (13) based on 2,703 psychiatric visits. Percents based on weighted sampling.

^bSignificantly different from Northeast and West ($p < 0.001$) and South ($p < 0.01$).

^cEstimate with relative standard error that exceeds 40%.

^dSignificantly different from Northeast ($p < 0.01$).

^eSignificantly different from Midwest ($p < 0.01$) and South ($p < 0.02$).

Extended visits had the longest mean duration (68.4 minutes), followed by standard visits (47.5 minutes) and diagnostic interviews (47.3 minutes). By definition, medication visits (mean=13.7 minutes) and brief visits (mean=25.5 minutes) were the shortest types of visits.

Type of Practice

Nearly three-quarters (72.5%) of the visits were to psychiatrists in solo practice. The remaining visits were distributed among psychiatrists in group practice (17.6%) and psychiatrists in partnerships or other practice arrangements (9.8%).

Most of the visits provided by psychiatrists in solo practice were standard visits. In contrast, less than a third of the visits provided by psychiatrists in group practice were standard visits. Compared to solo practitioners, psychiatrists in group practice provided a significantly larger proportion of their visits as diagnostic interviews, medication visits, and brief visits (table 1).

Subspecialization

The vast majority of the psychiatric visits were to general psychiatrists (77.8%). A substantially smaller proportion were to psychiatric subspecialists such as psychoanalysts (12.1%), child psychiatrists (8.5%) or other subspecialists (1.6%).

Standard visits accounted for a substantially larger proportion of the visits provided by psychiatric subspecialists (77.8%) than by general psychiatrists (47.8%) ($p < 0.01$). In contrast, medication visits (8.5% versus 0.3%), brief visits (24.8% versus 6.1%), and extended visits (10.5% versus 6.7%, $p < 0.01$) each accounted for a larger percentage of the visits to general psychiatrists than to psychiatric subspecialists. Diagnostic interviews accounted for a nearly even proportion of the visits provided by the two physician groups (general psychiatrists: 8.7%, psychiatric subspecialists: 9.1%).

Geographic Region

Psychiatric visits tended to be concentrated in the Northeast. The estimated rate of psychiatric office visits per 1,000 noninstitutionalized civilians was 127 in the

TABLE 3. Demographic Characteristics of Patients Making Office Visits to Psychiatrists^a

Patient Variable	Percent				
	Diagnostic Interviews	Medication Visits	Brief Visits	Standard Visits	Extended Visits
Age (years)					
<18	9.4 ^b	3.7 ^b	3.7 ^b	7.4	7.3 ^b
18-35	39.8	27.6	31.5	40.0 ^c	33.7
36-50	26.9	28.9	29.4	37.2	45.3 ^d
51-65	17.7	19.8	24.4 ^e	12.5	12.9
>65	6.1 ^b	20.0 ^e	10.9 ^e	2.8	0.8 ^b
Mean	38.3	44.1	44.3	36.3	37.8
Sex					
Female	57.8	57.7	63.6	58.2	59.9
Male	42.2	42.3	36.4	41.8	40.1
Race					
White	94.3	92.3	87.0	98.3	97.6
Nonwhite	5.7 ^b	7.7 ^b	13.0	1.7 ^b	2.4 ^b
Payment source					
Self-payment	44.2	43.8	43.2	65.1 ^f	62.7
Commercial insurance	37.5	23.7	36.8	49.6 ^g	49.9
Medicare	4.8 ^b	17.1	12.7 ^e	2.4	0.9 ^b
Medicaid	4.4 ^b	25.0	16.6	1.1 ^b	1.1 ^b
HMO/prepaid care	10.6 ^b	0.9 ^b	6.5 ^b	3.6	4.1 ^b

^aData from 1985 National Ambulatory Medical Care Survey (13) based on 2,703 psychiatric visits. Percents based on weighted sampling. More than one payment source was possible.

^bEstimate with relative standard error that exceeds 40%.

^cSignificantly different from medication visits ($p < 0.05$).

^dSignificantly different from diagnostic interviews ($p < 0.05$).

^eSignificantly different from standard visits ($p < 0.001$).

^fSignificantly different from brief visits ($p < 0.01$), medication visits ($p < 0.05$), and diagnostic interviews ($p < 0.05$).

^gSignificantly different from medication visits ($p < 0.001$) and brief visits ($p < 0.05$).

Northeast, 90 in the West, 67 in the Midwest, and 47 in the South.

The distribution of visit categories varied by geographic region. Although standard visits were the most common type of visit provided in each of the four geographic regions, standard visits were particularly common in the Northeast and West. Diagnostic interviews accounted for a significantly larger proportion of the visits in the Midwest than in the other regions. Brief visits were proportionately most common in the South and least common in the Northeast, where extended visits were also comparatively uncommon. Medication visits accounted for less than one-tenth of the visits in each geographic region (table 2).

Patient Demographics

Most of the visits were made by patients who were white (95.2%), female (59.4%), and between the ages of 25 and 44 years (56.2%) and who used either self-payment (57.1%) or commercial insurance (45.1%) to help pay for their visits.

Patients who received medication visits or brief visits tended to be older than patients who received other types of visits. Medication visits and brief visits also tended to be made by a disproportionately high percentage of nonwhite patients and patients who paid for their care with public financing.

Patients who made standard visits were significantly more likely than patients who made diagnostic interviews, brief visits, or medication visits to pay for their care with personal resources. Patients who made stand-

ard visits were also more likely than patients who made medication or brief visits to use commercial insurance (table 3).

Treatment

Psychotherapy, defined as a nonmedication treatment "designed to produce a mental or emotional response through suggestion, persuasion, reeducation, reassurance, or support" (13), was provided during the vast majority (88.7%) of visits. It was provided during approximately half of the medication visits and during more than two-thirds of the other types of visits (table 4).

Medications were prescribed in nearly half (46.3%) of the visits, and most of these prescriptions (85.4%) were for psychotropic medications. As expected, psychotropic medications were prescribed more commonly during medication visits than during any other type of visits. Psychotropic medications were also prescribed in a comparatively high percentage of brief visits (table 4).

The trends observed for the frequency of overall psychotropic medication prescription were also found for specific classes of medications. Antidepressants, anxiolytics, and particularly antipsychotics tended to be more commonly prescribed during medication visits and brief visits than during the other types of visits (table 4).

Diagnosis

The most common primary diagnoses were depressive disorders (29.4%), neurotic disorders (17.6%), psychoses (16.3%), and personality disorders (14.4%).

TABLE 4. Treatment Characteristics of Patients Making Office Visits to Psychiatrists^a

Treatment Variable	Percent				
	Diagnostic Interviews	Medication Visits	Brief Visits	Standard Visits	Extended Visits
Psychotherapy					
Provided	70.3	54.4	85.5 ^b	95.8 ^c	96.4 ^b
Not provided	29.7	45.6	14.5	4.2	3.6 ^d
Psychotropic medications					
Any	23.0	86.8 ^c	64.9 ^e	30.9	31.2
Antidepressants	12.7 ^d	38.6 ^f	39.3 ^g	16.6	23.0
Anxiolytics	4.5 ^d	30.9 ^h	23.0 ^h	9.3	7.9 ^d
Antipsychotics	3.2 ^d	41.8 ^h	29.2 ^h	6.5	5.7 ^d

^aData from 1985 National Ambulatory Medical Care Survey (13) based on 2,703 psychiatric visits. Percents based on weighted sampling.

^bSignificantly different from medication visits ($p < 0.05$).

^cSignificantly different from medication visits ($p < 0.01$).

^dEstimate with relative standard error that exceeds 40%.

^eSignificantly different from diagnostic interviews, standard visits, and extended visits ($p < 0.001$).

^fSignificantly different from standard visits ($p < 0.01$).

^gSignificantly different from standard visits ($p < 0.001$) and extended visits ($p < 0.01$).

^hSignificantly different from standard visits ($p < 0.001$).

TABLE 5. Diagnoses of Patients Making Office Visits to Psychiatrists^a

Diagnostic Group	Percent				
	Diagnostic Interviews	Medication Visits	Brief Visits	Standard Visits	Extended Visits
Psychotic disorder	9.0 ^b	43.3 ^c	32.8 ^c	9.3	8.2 ^b
Depressive disorder	22.2	27.4	34.0 ^d	28.6	31.8
Neurotic disorder	9.9 ^b	12.8 ^b	10.6	21.4 ^e	21.7 ^f
Personality disorder	7.2 ^b	3.9 ^b	3.7 ^b	20.7	15.6
Adjustment disorder	16.9 ^g	3.0 ^b	8.6	8.1	14.0 ^b
Substance abuse	11.2 ^b	0.4 ^b	2.0 ^b	0.4 ^b	0.6 ^b
Other	23.6 ^h	9.2 ^b	8.3	11.5	8.1 ^b

^aData from 1985 National Ambulatory Medical Care Survey (13) based on 2,703 psychiatric visits. Percents based on weighted sampling.

^bEstimate with relative standard error that exceeds 40%.

^cSignificantly different from standard visits ($p < 0.001$).

^dSignificantly different from diagnostic interviews ($p < 0.05$).

^eSignificantly different from brief visits ($p < 0.001$).

^fSignificantly different from brief visits ($p < 0.01$).

^gSignificantly different from brief visits and standard visits ($p < 0.01$).

^hSignificantly different from brief visits ($p < 0.001$) and standard visits ($p < 0.01$).

Adjustment disorders (9.2%), substance abuse-related disorders (1.7%), and other disorders (11.4%) were less common.

More than one-third of the medication visits and nearly a third of the brief visits were to patients diagnosed with a psychotic disorder. In contrast, fewer than a tenth of the other types of visits were to patients with psychotic disorder diagnoses (table 5).

Personality disorders and neurotic disorders tended to be diagnosed during a larger proportion of standard visits and extended visits than during other types of visits. Adjustment disorders and substance abuse disorders tended to be diagnosed in a larger percentage of diagnostic interviews than in other types of visits (table 5).

Medication Visits

A logistic regression was performed to examine the association between selected demographic, clinical, and practice variables and the occurrence of a medication visit. Visits to general psychiatrists were nearly 20 times more likely than visits to psychiatric subspecialists to be medi-

cation visits. Payment with public funds, patient age over 65, and the prescription of an antipsychotic medication also increased the likelihood of a medication visit. Patients who received psychotic disorder diagnoses were at a slightly higher risk of receiving a medication visit than patients with other diagnoses (table 6).

Brief Visits

The relative risk of receiving a brief visit was increased if the visit was made by a patient who was of nonwhite racial background, was over 65 years of age, or paid with public funds. Physician subspecialization, type of practice, geographic location, patient diagnosis, and neuroleptic medication prescription also significantly influenced the probability of a brief psychiatric visit (table 7).

DISCUSSION

A stereotyped view of private practice psychiatry assumes that psychiatrists devote their time nearly exclu-

TABLE 6. Demographic, Treatment, and Practice Risk Factors for Medication Visits^a

Variable ^b	Odds Ratio ^c	95% Confidence Interval
Age (>65 years versus <65 years)	3.12	1.98–4.94
Sex (male versus female)	1.10	0.79–1.53
Race (white versus nonwhite)	1.70	0.85–3.41
Medication (neuroleptic versus no neuroleptic)	2.90	1.91–4.41
Diagnosis (psychotic disorder versus other disorders)	1.63	1.07–2.49
Subspecialty (absent versus present)	18.61	4.55–76.16
Payment (public versus other) ^d	4.53	2.92–7.03
Type of practice (solo versus nonsolo)	1.19	0.82–1.72
Region (Midwest versus other)	1.26	0.79–2.00

^aData from 1985 National Ambulatory Medical Care Survey (13) based on 2,703 psychiatric visits.

^bHigher risk group is listed first in parenthesis.

^cOdds ratio estimates relative risk.

^dPublic payment includes Medicare or Medicaid.

sively to the provision of "psychotherapy hours." In fact, the reality is considerably more complex. Psychiatrists provide a broad mix of outpatient clinical services.

In an effort to contain expenditures, third-party payers have developed payment schedules that distinguish various types of office-based psychiatric visits. The most common system for categorizing visits is the CPT (3), and the most influential payment schedule is the Medicare schedule. If recently introduced changes in the Medicare schedule are adopted by other third-party payers, the economics of private practice psychiatry will be significantly altered.

Medication Management

In 1985, medication management visits accounted for an estimated 6.7% of office-based psychiatric visits. Since 1985, Medicare has reduced patient copayments for medication management services and eliminated dollar limits. However, in some locales, the RBRVS has reduced physician fees for these visits. The changes in copayments should increase the demand for medication management visits, but the incentive to provide this service might fall if the fee falls too low. We do not know precisely what to expect, but it would be unfortunate if a policy designed to increase access to services for the "medical management" of mental disorders was foiled by another policy designed to improve fees for "cognitive services" for the same Medicare beneficiaries.

Medication management visits are provided to a particularly vulnerable patient population. Older patients and those who receive antipsychotic medication, suffer from psychotic disorders, or pay for services with public funds are all disproportionately reliant on medication management visits. Fee schedules that do not sufficiently reward physicians for their efforts to treat this patient population may further exacerbate the problem of undertreatment. Epidemiologic evidence suggests that a substantial proportion of persons with the most

TABLE 7. Demographic, Treatment, and Practice Risk Factors for Brief Psychiatric Visits^a

Variable ^b	Odds Ratio ^c	95% Confidence Interval
Age (>65 years versus <65 years)	3.08	2.45–4.85
Sex (female versus male)	1.03	0.84–1.27
Race (nonwhite versus white)	2.46	1.62–3.73
Medication (neuroleptic versus no neuroleptic)	1.91	1.41–2.57
Diagnosis (psychotic disorder versus other disorders)	1.61	1.21–2.15
Subspecialty (absent versus present)	2.38	1.72–3.29
Payment (public versus other) ^d	2.26	1.56–3.27
Type of practice (nonsolo versus solo)	2.08	1.69–2.57
Region (South versus other)	1.64	1.31–2.06

^aData from 1985 National Ambulatory Medical Care Survey (13) based on 2,703 psychiatric visits.

^bHigher risk group is listed first in parenthesis.

^cOdds ratio estimates relative risk.

^dPublic payment includes Medicare or Medicaid.

severe mental disorders do not receive mental health treatment (14).

Brief Visits

In an effort to correct what was deemed as excessive physician fees for shorter office visits, the RBRVS significantly reduced physician fees in several locales for individual medical psychotherapy visits of approximately 20 to 30 minutes in length (CPT code 90844). These brief visits account for approximately one-fifth of visits to office-based psychiatrists.

Certain groups of psychiatrists rely more heavily than others on the provision of brief visits. This group includes general psychiatrists; psychiatrists in group practices, partnerships, or other nonsolo arrangements; and those who practice in the South. These psychiatrists are the most vulnerable financially to fee reductions for brief visits.

The overall public health consequences of reducing patient charges and physician fees for brief visits depend upon how patients and psychiatrists respond. Because utilization of outpatient mental health services is highly price sensitive (15, 16), lowering out-of-pocket expenses may increase patient demand.

How psychiatrists will respond to a cut in reimbursement is less certain. If psychiatrists are willing to see patients during brief visits at reduced fees, brief visits will remain common. If psychiatrists respond by broadening their range of clinical activities and shifting to more lucrative services (17), a shortage may develop in the provision of brief visits. This shortage would have the greatest impact on nonwhite patients, older patients, publicly financed patients, and patients with psychotic disorders.

Other Visits

Depending somewhat on the locale, the new Medicare RBRVS pays physicians for longer outpatient psy-

chiatric services at rates that differ only modestly from historical rates. These visits, which we consider as psychiatric interviews, standard visits, and extended visits, account for a majority of the patient contacts in office-based psychiatric practice.

Patients who receive these longer visits tend to be less severely ill than those who receive shorter visits. Psychotic disorders, for example, are diagnosed in a comparatively small proportion of standard or extended visits. This finding may relate to the consistently negative results of intensive psychotherapy for schizophrenia and other psychotic disorders (18). In other psychiatric conditions, such as depressive disorders (19) and various anxiety disorders (20), the role of more extensive psychotherapeutic interventions is more well established (21, 22).

A small but significant percentage of office-based psychiatric visits exceed 55 minutes in length. The demographic and diagnostic composition of patients who receive extended visits closely resembles that of patients who receive standard visits. Under current CPT coding, psychiatrists have no means of billing for the added effort and expense involved in providing extended visits. If mental health researchers can clearly define the conditions under which extended visits are medically necessary, such as the assessment of acutely dangerous patients, then a rational payment policy can be developed to compensate psychiatrists for their added clinical efforts. Without precise indications for extended visits, it is unlikely that third-party payers will assume the added financial risk of reimbursing these visits at higher than standard rates.

Overview

Rational health care policies seek to promote access to treatment for those in need while controlling overall costs. With the increased differentiation of reimbursement for outpatient psychiatric services, concern has developed that coverage for traditional psychotherapy will be carved out. In fact, the new Medicare RBRVS system may well have the opposite effect. In some areas, sharp reductions in fees for shorter visits threaten to decrease the financial incentives to provide these services, while the relative preservation of fees for longer psychotherapy visits makes these services comparatively more remunerative.

The U.S. mental health care system has been described as two-tiered: one for those with insurance and one for the poor and severely disabled (23). An important criterion for evaluating the success of psychiatric reimbursement policies remains the extent to which they promote equity of access and coverage for those in greatest need.

We have just entered a period of substantial change in the payment for ambulatory psychiatric services. Cost increases and the imposition of a fee schedule could threaten the few gains made in the financing of care for individuals with mental disorders. Future studies should examine the

impact of these changes in policy on trends in the mix of patients served, the content of services, and the pattern of psychiatric outpatient practice.

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A National Study of Psychiatrists' Professional Activities

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***Objective and Method:** A mail survey was conducted in 1988–1989 to study the professional activities of U.S. psychiatrists. Data from the 19,431 active respondents are reported. **Results:** Nineteen percent of the psychiatrists were women, an increase from the 17% reported in 1982. The median age of the respondents was 50 years. Nearly one-third of the respondents expressed interest in each of the following areas of subspecialization: adolescent psychiatry, substance abuse, geriatrics, and consultation-liaison psychiatry. More than one-fifth reported formal fellowship training in child/adolescent psychiatry. The psychiatrists worked an average of 48 hours per week—two-thirds in direct patient care—in an average of 2.3 different settings. The proportion of psychiatrists reporting private practice as their primary work setting showed a marked decline from 53% in 1982 to 45% in 1988. There was an increase from 4% in 1982 to 11% in 1988 in those whose primary work setting was a private psychiatric hospital. The typical caseload was over 60 patients, with roughly half that number seen each week. For inpatients treated, the two most common diagnoses were affective disorders and schizophrenic disorders. In a typical week psychiatrists treated about one-half of their outpatients with individual psychotherapy; three-fifths of these were also treated with medications. The average net income for psychiatrists working 35 hours or more per week was \$99,850 for men and \$73,174 for women. **Conclusions:** Major trends evident from this study are subspecialization, medicalization, privatization, feminization, and organizational diversification.*

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In psychiatry, as in other medical specialties, the 1990s are a time of transition toward new patterns of activities as the profession adapts to rapidly changing socioeconomic and scientific influences. In the 1980s, advances in treatments, new forms of economic pressures on practice, and a changing mix of characteristics of practitioners, work settings, training, and roles characterized psychiatry (1, 2). To describe better these changes in practice, APA periodically conducts a national census survey of active psychiatrists (defined in detail below) in the United States (3, 4). Reports based

on earlier surveys (5–9) provide a useful background for understanding the present findings. This article reports findings from the ninth, and most recent, study describing psychiatrists' current professional activities, conducted in 1988–1989. The study, supported by APA, was designed and overseen by the Committee on the Biographical Directory and Research on Psychiatric Professional Activities.

This article provides a picture of psychiatrists' professional activities in 1988 and selectively makes comparisons with earlier studies to illustrate trends. For example, the proportion of women practitioners is higher in psychiatry than in most other medical specialties. The proportion of women among active psychiatrists increased by more than 50% between 1965 and 1982, and we found evidence that this trend is continuing (10). Also, because of federal health manpower policies that during the 1970s encouraged medical students to enter psychiatry as a career, we expected to see some evidence of a "resident boom" reflected in the number of middle-aged psychiatrists among currently active practitioners.

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Major support for this survey was from the APA Committee on the Biographical Directory and Research on Psychiatric Professional Activities. It was supported also in part by NIMH Scientist Development Award MH-00848 to Harvard University (Dr. Dorwart).

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METHOD

The Professional Activities Survey was conducted in two phases: APA members were surveyed in 1988 and nonmember psychiatrists in 1989. The member population was defined by the list of all psychiatrists who were APA members in 1988. The total number of members at the time of the survey was 34,164. The number of members responding to the survey was 23,126, or 67.7%. The nonmember population was identified from an American Medical Association list of all U.S. physicians who had identified themselves as specializing primarily in psychiatry. That list was then cross-checked against the APA membership file and duplications eliminated. The result was a residual list of 10,091 self-designated psychiatrists who were not members of APA; questionnaires were mailed to everyone on this list. Some 2,922 completed forms were returned by this group, for an unadjusted response rate of 28.9%. Thus, a total of 26,048 responses were received from member and nonmember respondents. Of the 2,922 nonmember respondents, 341 reported that they were not psychiatrists, and it was determined that 125 were APA members mistakenly included in the nonmember list. In this study, an "active psychiatrist" is defined as one who is neither retired nor a resident/fellow and who is principally engaged in the practice of psychiatry. Combining member and nonmember responses from only the active psychiatrists yielded data on 19,431 active respondents for analysis. For convenience, throughout this article when we use the term "psychiatrists," we are referring to active psychiatrist respondents to our survey.

Some "core" questions appeared on every questionnaire distributed. Others, designated "special topics" questions, were distributed only to subsamples. Each subsample was composed of one-fifth of the total survey population. Some special topics questions were sent to only one subsample and others to two. There were five special topics: treating chronic mental illness, patients' characteristics (diagnoses and demographics), hospital affiliations, economics of practice, and referral patterns.

There are several limitations of this study that should be noted. First, in any survey there is the possibility of response bias. An analysis of demographic characteristics in which respondents were compared with nonrespondents, APA members with nonmembers, and special topics respondents with the entire group of respondents revealed no major differences. Nonetheless, the low response rates of psychiatrists who were not APA members and also for selected items, such as income, are of concern. While they are comparable to response rates for similar independent surveys of physicians' income, these low figures warrant caution. The resulting average incomes, for instance, may be downwardly biased.

Another problem arises when a smaller subsample of respondents answers questions about activities of low frequency, such as the use of specific treatment modalities (e.g., couples therapy or biofeedback). Other limi-

tations of survey methodology inherent in our data involve self-reporting with respect to clinical diagnoses of patients treated, recollection and estimation of weekly or monthly activities, and so forth. In some cases (e.g., specialty board certification), we obtained independent data to validate the accuracy of responses. Although many multipart questions yielded slightly different sample sizes for each item, there remained a large total number of responses to nearly every item.

RESULTS

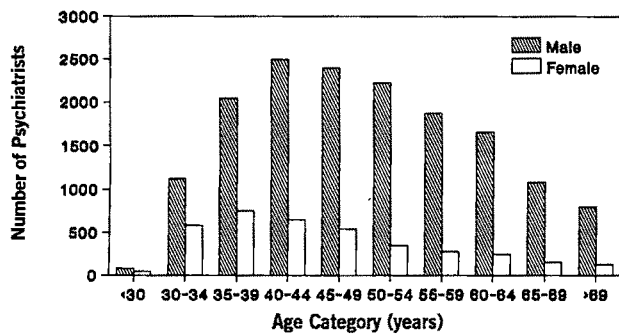
Demographic Characteristics of Active Psychiatrists

In this survey, 19.1% of the active respondents were women; this compares with 17.3% of the respondents in the 1982 survey of psychiatrists (3, 9). The trend toward an increasing proportion of women in psychiatry is underscored by another study which found that 41% of psychiatric residents in 1987-1988 were women (10). Minorities accounted for 14.6% of the respondents to the present survey, with a slightly higher representation among nonmembers. Asians constituted 8.9%, Hispanics 4.1%, blacks 1.6%, and Native Americans 0.17%. This distribution had changed little from 1982; only the proportion of Asians was up slightly, from 8.3% then. The median age of the psychiatrists in our survey was 49.6 years. This was virtually unchanged from the 1982 APA survey.

Figure 1 presents data on the distribution of active psychiatrists by age category and by gender in 1988. Fewer than 10% of active psychiatrists (excluding residents) were younger than 35 years, and just over 10% were over 65; more than 50% were between 35 and 54. Although the groups are not entirely comparable because of differences in size, a greater proportion of psychiatrists than of general physicians appear to be in the middle age range, with fewer in the younger (below 35) and the older (above 65) categories. Comparing active respondents from the APA surveys of 1988 and 1982 by age group and gender, we found smaller proportions of psychiatrists below the age of 40 and greater proportions between 60 and 69 in the 1988 survey. We also found greater proportions of women in the younger age categories in 1988 than in 1982 (there were few active practitioners younger than 30 in our sample). The "bulge" in the distribution's middle-aged categories (35-50 years) reflects increased numbers of physicians entering the field in the 1960s and 1970s.

Geographic Distribution of Psychiatrists

Over the past 40 years, the numbers of physicians and psychiatrists in the United States have steadily increased, not only in terms of absolute numbers but also in terms of the ratio of physicians to population. For example, in 1970 there were approximately 10 psychiatrists per 100,000 population, and this had increased to roughly 17 per 100,000 by 1988. The dis-

FIGURE 1. Ages of 19,431 Active Psychiatrists Who Responded to a Survey Questionnaire

tribution and rates of growth vary unevenly by region of the country and by state or metropolitan area (3). The psychiatrists we surveyed were disproportionately located in several large urban areas; more than one-fourth of the active respondents were practicing in New York (15.7%) and California (13.0%), while fewer than 1% of all psychiatrists who responded practiced in six rural states. Table 1 illustrates the variation in the ratios of responding active psychiatrists to the populations in regions of the United States, ranging from a low of 3.5 per 100,000 in the southeast to a high of 15.9 in New England.

Specialization in Psychiatry

One of the cardinal features of growth and change in psychiatry in the 1980s was a trend toward subspecialization. We collected several kinds of information that permit us to document this trend: data on training, certification, subspecialty interests of members, types of patients treated, and settings in which psychiatrists work.

Not surprisingly, we found that members' subspecialty organizational affiliations and clinical interests extended beyond formal subspecialty fellowship training, although for child psychiatry there was a rough correspondence in the total number who had formal training (20.9%) and the number who were members of the American Academy of Child and Adolescent Psychiatry (20.5%). Of respondents who expressed *interest* in a subspecialty, more than 30% indicated adolescent psychiatry, alcohol abuse, consultation-liaison, or geriatric psychiatry as the area of interest; more than 20% indicated administrative psychiatry, child psychiatry, or forensic psychiatry. An interest in research was expressed by 12.8%, while 3.0% reported having at least 1 year of formal training in research. Two other established formal subspecialty areas (in which respondents had fellowships of at least 1 year) were administrative and community psychiatry (1.4%) and consultation-liaison psychiatry (1.5%). Newer specialties had small but growing representation among formal subspecialty fellowship trainees: forensic, 0.7%; geriatric, 0.7%; and substance abuse, 0.4%.

TABLE 1. Active Psychiatrists in Regions of the United States in 1988 According to 19,183 Survey Respondents

Region ^a	Number of Psychiatrists	Population (in thousands) ^b	Ratio ^c
Southwest central	1,278	26,885	4.8
Northeast central	2,438	42,119	5.8
Northwest central	943	17,759	5.3
Pacific	3,395	37,351	9.1
Southeast central	544	15,344	3.5
South Atlantic	2,937	41,809	7.0
Mountain	836	13,328	6.3
Middle Atlantic	4,753	37,631	12.6
New England	2,059	12,963	15.9

^aThis regional analysis excludes the District of Columbia.

^bRegional population estimates for 1988 were taken from the *Statistical Abstract of the United States, 1990*.

^cRatios are based on the number of active, responding psychiatrists per 100,000 resident population.

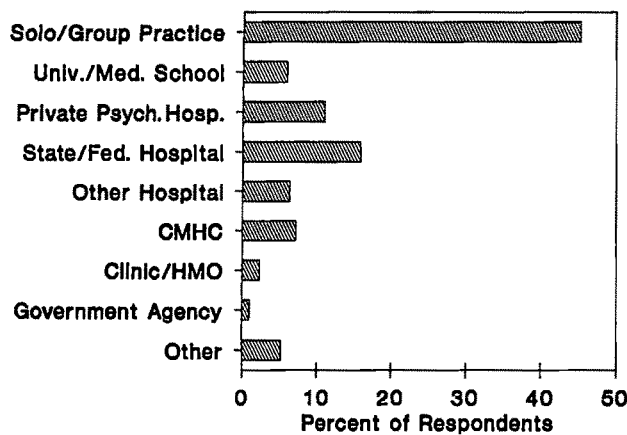
Many psychiatrists pursue their subspecialty interests through participation in specialty societies or organizations, including training that is not necessarily full-time fellowship education. To illustrate, 7.2% were members of the American Academy of Psychiatry and the Law, 4.2% belonged to the American Academy of Psychiatrists in Alcoholism and Addictions, and 5.2% were members of the American Association for Geriatric Psychiatry. Approximately 8% also belonged to the American Society for Adolescent Psychiatry and 20.7% to the American Psychoanalytic Association and the American Academy of Psychoanalysis combined. Cross-membership in organizations such as the American College of Neuropsychopharmacology (1.7%) or the Society of Biological Psychiatry (3.5%) is consistent with the research interests of many psychiatrists. Affiliation with the following other scholarly or professional organizations reflects not specialty orientation per se but, rather, broad identification with medicine or other aspects of the profession: American Medical Association (56.4%), American College of Psychiatrists (6.1%), American Orthopsychiatric Association (7.6%), and Group for the Advancement of Psychiatry (4.0%).

Practice Activities of Psychiatrists: Settings and Time

Psychiatrists worked in a wide variety of settings, and most worked in more than one setting. The mean number of settings was 2.3 in 1988, as it was in 1982. For example, a psychiatrist might work half the time in a medical school, involved in teaching and research, and one-quarter of the time in a local community mental health center (CMHC) and also maintain a part-time private office practice and be a consultant to a nursing home. In general, psychiatrists' practices have been characterized over the past 25 years by a predominance of private practice over other primary work settings and by a large and growing involvement in organization-based practice (11, 12, 13 [p. 81]).

In 1988 the proportion of psychiatrists reporting private practice, alone or in an office-based group, as their primary activity (i.e., the setting where they worked the

FIGURE 2. Primary Work Settings of 19,431 Active Psychiatrists Who Responded to a Survey Questionnaire



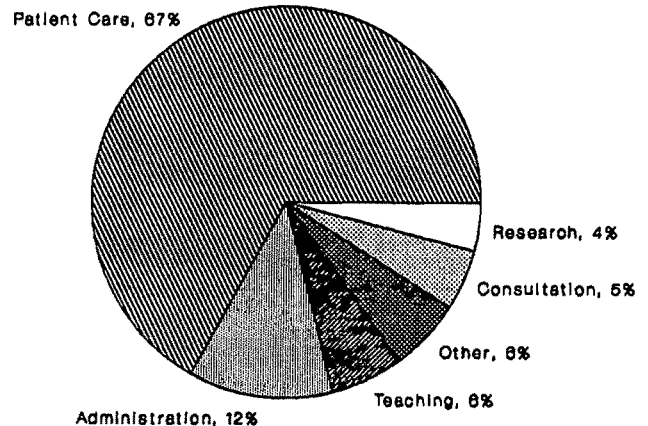
greatest number of hours in a typical week) was 45.1%, compared to 57.7% in 1982 (figure 2). On the other hand, private office practice remained the second most common secondary work setting, with 25.8% of the respondents reporting this in 1988. In contrast to the reduction in private practice, the proportion of psychiatrists who worked in private, free-standing, specialty psychiatric hospitals rose from 3.7% in 1982 to 11.4% in 1988. The proportion in *solo* private practice was 38.2% in 1988. Nearly 16% of all respondents indicated a state hospital as their primary work setting. Of the active respondents, 26.5% worked exclusively in one setting, while 37.9% worked in three or more settings per week. One of the most common patterns among psychiatrists was to combine organizational work with a part-time private practice. Those who worked in private and other (primarily general) hospitals were the most likely to have a part-time private practice.

Figure 3 shows how psychiatrists allocated their time. The average paid work week for psychiatrists was 48 hours, unchanged since earlier studies in 1982 and 1970. Direct patient care occupied more than two-thirds (67%) of all work time for psychiatrists. Time devoted to other professional activities, such as administration, teaching, consultation, and research, is also shown in figure 3. An *additional* 8 hours per week of professional activity was unpaid.

Trends in Patient Characteristics and Treatment Modalities

Respondents reported a mean of 32.6 hours of direct patient care per week; the median was 34 hours. Again, this represents two-thirds of all professional effort (figure 3). These figures vary across work settings, thus affecting the average number of patients seen in different work settings. Considering only patients treated in the respondents' primary work setting, we found that psychiatrists whose primary work setting was a CMHC treated the largest number of patients per week, an average of 35 patients. Psychiatrists whose primary work

FIGURE 3. Percentages of Time Spent in Professional Activities by 19,431 Active Psychiatrists Who Responded to a Survey Questionnaire



setting was a private office practice or a health maintenance organization (HMO) treated an average of 30 patients per week, compared to 20 per week treated by psychiatrists working primarily with inpatients in private psychiatric hospitals. The significance of this difference for the quality of care rendered is unknown; some of the divergence is probably caused by differences in the proportion of patients requiring individual psychotherapy and to differences in psychiatrists' non-clinical responsibilities in public versus private settings. Psychiatrists whose primary work setting was a medical school or a government agency treated the smallest numbers of patients per week, approximately 11 and six patients, respectively. This is most likely because of their other professional responsibilities, such as teaching, administration, and research. The number of patients seen per week in 1988 in most settings was quite similar to the number reported in the 1982 APA survey (13).

Treatment Settings

Treatment settings can be grouped into outpatient, inpatient, and partial hospitalization categories. The figures represent the average caseloads of all psychiatrists who reported treating *any* patients in a given kind of treatment setting, not the caseloads of psychiatrists whose primary workplace was one of these settings. Psychiatrists treated a mean monthly caseload (different patients seen at least once) of 47 patients (median=35) in outpatient settings. They saw a mean monthly caseload of 31 different patients (median=22) in inpatient settings and a mean of 21 different patients (median=11) in partial hospitalization settings. Because the intensity of service is typically greater in inpatient and partial hospitalization settings, psychiatrists carry smaller monthly caseloads in these settings.

When patients seen at least once during the preceding month were grouped according to their principal diagnosis, the five most common diagnostic categories

among outpatients were affective disorders (26.3%), anxiety disorders (14.3%), schizophrenic disorders (12.6%), personality disorders (11.0%), and adjustment disorders (7.9%). The five most common diagnoses among inpatients were affective disorders (21.2%), schizophrenic disorders (17.9%), alcohol-related disorders (9.4%), personality disorders (8.4%), and organic mental disorders (8.2%). In partial hospitalization settings, the five most common diagnostic groups were schizophrenic disorders (30.2%), affective disorders (15.9%), disorders of childhood (11.1%), developmental disorders (9.1%), and personality disorders (7.1%). Figure 4 shows the distribution of diagnoses in the three kinds of settings combined. The validity and reliability of these diagnoses is unknown, since they are based on psychiatrists' self-reports. However, patients with schizophrenia, who represent only 5% of individuals with diagnosable mental disorders (14), represented a much larger proportion of the responding psychiatrists' caseloads.

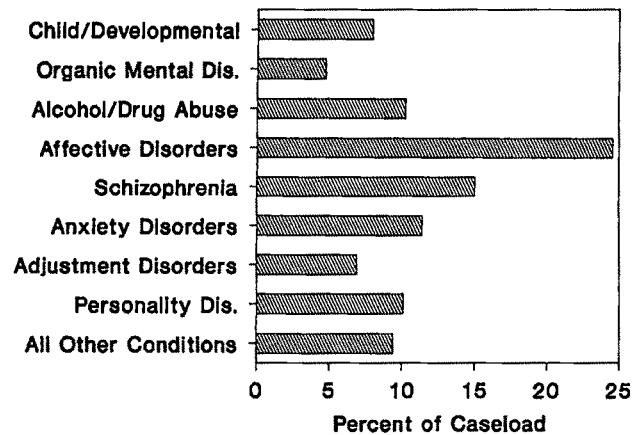
In outpatient settings, during a typical work week psychiatrists treated about one-half (52.1%) of their patients with individual psychotherapy; of these patients, three-fifths (60.5%) were also treated with medications. About one in six patients (17.9%) received medication management alone. More than half (54.5%) of the psychiatrists' patients received pharmacological treatment, alone or combined with psychotherapy. About one in seven outpatients (14.6%) was seen for assessment and evaluation, which may or may not have led to further treatment. Psychiatrists' medical training is essential for both pharmacotherapy and the evaluation of new patients, which together involved more than two-thirds of their outpatients. Contrary to popular perception, only 2.7% of psychiatrists' outpatients were engaged in psychoanalysis. About one in 25 outpatients (4.3%) participated in group psychotherapy and a similar proportion (4.2%) in couples therapy.

ECT was rarely administered on an outpatient basis (0.5% of patients), which is consistent with the APA task force recommendation that this treatment be reserved for "a carefully selected population of patients" (15, p. 34). Fewer than one in 10 psychiatrists (7.4%) nationwide had utilized ECT in the month before responding to the 1988 survey (roughly 6% of the total sample had used ECT for five or fewer patients, and about 1% had used ECT with a greater number of patients). Less than one-tenth of one percent of outpatients were treated with ECT.

Psychiatrists' Incomes

Psychiatrists' incomes are often reported to be lower than those of most other medical specialties; however, these reports mask wide variations (16). We asked respondents to report salaried and nonsalaried income and professional expenses. We calculated the mean annual income of psychiatrists practicing more than 35 hours per week. For men the mean net income in 1988 was \$99,850 (in 1988 dollars), and for women the

FIGURE 4. Distribution of Caseloads, by Diagnostic Category, of 19,431 Active Psychiatrists Who Responded to a Survey Questionnaire



mean was \$73,174. Besides the marked differences by gender, there were also wide differences by region of the country and by primary work setting. To illustrate, for male psychiatrists working 35 hours or more, the mean net income in the southwest central region was roughly \$105,000 annually, compared to approximately \$85,000 in the northeast. According to primary work setting, private practitioners reflected the mean (\$99,864), while those in private psychiatric hospitals earned \$116,000, and those in state or federal hospitals reported a lower mean income (\$84,000).

DISCUSSION

Psychiatry shares with other medical subspecialties a predominant reliance on private practice as the major setting and form of activity. However, the growth of other settings for practice, such as hospitals, HMOs, preferred provider organizations (PPOs), and group practices, could be expected to reduce reliance on office-based private practice. We therefore expected to see evidence of changes in primary work settings and to see increasing subspecialization in clinicians' training, interests, types of patients treated, and modalities of therapy used. We were also interested in influences related to major changes in the financing and organization of care, such as the impact of growing competition on psychiatric practice and on incomes of psychiatrists (11). Our results represent more than isolated changes, for we see several major trends influencing professional practice that are likely to continue in the 1990s. For example, a combination of sociodemographic, scientific, economic, organizational, and professional forces have converged to bring about the current growth of psychiatric subspecialization in geriatrics, addictions, and other fields. We review and discuss here some of the trends and implications of the major findings of our survey.

1. Feminization. As psychiatry grows, new demo-

graphic patterns are emerging. Most strikingly, more women are entering psychiatry than ever before, a trend some observers have called "feminization." Actually, more women are entering medicine generally, and several specialties (e.g., pediatrics, obstetrics/gynecology) are experiencing increases in the proportions of young women in those fields. Because of an increase in the average age of practitioners in psychiatry, this increased attraction of women into the profession seems fortunate. This trend toward older practitioners undoubtedly reflects a gradual decline in interest in careers in psychiatry following a peak in the 1960s and 1970s. These trends deserve further attention from researchers in the future.

Future research should explore these findings in more depth. For example, because of recent entry into active practice, women in psychiatry are disproportionately in the younger age categories. Is that why women report significantly lower average annual net salaries than do men? Or is it because, on average, women in the middle-aged categories work 10% fewer paid hours per week than do their male counterparts? In our survey, women were overrepresented in the younger age category, were slightly overrepresented among those who were salaried, and worked more frequently in the public sector (e.g., women were represented 2:1 in CMHCs). In terms of types of patients seen, female psychiatrists see more children and adolescents and fewer patients with substance abuse disorders. It is also possible that with all employment characteristics held constant, women are paid less because of gender and/or age bias. A thorough analysis of these sorts of differences is beyond the scope of this article. The issue, however, deserves further attention.

2. Organizational diversification. We found a decline in the proportion of psychiatrists who consider private office-based practice their primary work setting. At the same time, there has been an increase in the proportion whose primary work setting is in an organization. These findings result from several concurrent trends influencing health care generally. During the 1980s there was a dramatic growth in HMOs, PPOs, and group practices, which undoubtedly underlies some of the decline in solo private office practice (17). There was also a dramatic increase during the 1980s both in the number of private psychiatric hospitals and in the number of psychiatric units in general hospitals (18). Thus, underlying the trend toward greater involvement of psychiatrists in hospitals seem to be the larger trends of privatization and medicalization.

Significantly, psychiatrists continue to treat patients who have severe mental illnesses, such as schizophrenia and major depression. Altogether, our data reveal that a majority of patients seen by psychiatrists have some sort of "medical" involvement, such as taking psychiatric medications, requiring biomedical diagnostic tests, receiving other somatic therapies, or, in the case of patients with co-occurring medical conditions, receiving consultation. Psychiatric work in hospital settings, including private facilities, is increasing. There

is, simultaneously, an increase in psychiatrists' involvement (numerically and proportionately) in public settings, such as state, county, and municipal mental hospitals, Department of Veterans Affairs hospitals, and CMHCs. In all, public settings as the primary work site were reported by 25.0% of the psychiatrists, while 33.1% reported some type of hospital as their primary work setting.

3. Subspecialization. Our findings document the widespread impression of growing subspecialization in psychiatry. Our respondents frequently indicated multiple subspecialty interests, formal fellowship training, extensive membership in subspecialty organizations, and a considerable number of patients seen weekly in particular categories involving special skills, such as treatment of children, substance-abusing inpatients, or the elderly. For example, in terms of expressed subspecialty interests (primary, secondary, or tertiary), about 20% of the respondents mentioned child psychiatry and about 30% geriatric psychiatry. Psychoanalysis, substance abuse, and forensic psychiatry also had significant representation. Subspecialization has long been evident in the scientific and clinical pursuits of psychiatrists; however, recently there has been an accelerating trend toward formalization of subspecialties (19). In April 1991 the American Board of Psychiatry and Neurology gave its first examination to confer a certificate of added qualifications in geriatric psychiatry. Several other subspecialties (e.g., addictions, forensic psychiatry, administrative psychiatry, adolescent psychiatry, and consultation-liaison psychiatry) have requested similar status.

Additionally, in terms of professional roles, administration and research may be viewed as important subspecialties within psychiatry. Eleven percent of all professional time of psychiatrists is reportedly devoted to administration; 1.4% of the respondents reported fellowship training in administration, and APA has a separate certifying board for this activity. Administration is an important primary function of many psychiatrists, especially in public mental health agencies. As for research, 80% of the psychiatrists reported no such activity; however, about 20% spent at least 1 hour weekly. More meaningfully, 1.6% devoted 20 hours or more per week to research. Finding ways to increase entry into, training in, and long-term support for substantial research careers should be a high priority for advancement of the field.

CONCLUSIONS

The 1990s, the "decade of the brain" (20), portend rapid changes in the science and practice of psychiatry. The many changes in professional activities that are familiar to practicing psychiatrists are also documented in the patterns and trends found in this study. New treatments imply new forms of training and new ways to meet clinical needs of patients. Rapid changes in the financing and organization of care require individuals

as well as organizations to adapt to new health care delivery systems. In sum, we see evidence of more specialization and medicalization of clinical practice, more diversification of practice settings, and increased involvement in systems of organized care; private practice continues to decline as a primary work setting. More women are entering the field, and this trend will undoubtedly influence the profession in ways yet to be seen. It is therefore important that researchers of psychiatric services be prepared to monitor and analyze the magnitude and direction of future changes in psychiatric practice.

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Regional Cerebral Glucose Metabolism in Bulimia Nervosa

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Anna C. King, Julio Lucinio, M.D., and Robert M. Cohen, M.D., Ph.D.

***Objective:** The authors' purpose in this study was to further delineate the character of cerebral metabolism in bulimia nervosa and to determine if functional links could be made between regional cerebral metabolism and the symptoms of depression, obsessive-compulsive disorder, and bulimia nervosa. **Method:** Regional cerebral glucose metabolism was measured by using positron emission tomography in 11 inpatients with bulimia nervosa and 18 normal comparison subjects matched in sex (all were women), age, and educational level. The bulimic patients were also tested for symptoms of major depression and obsessive-compulsive disorder. **Results:** The patients with bulimia showed a correlation between lower left anterolateral prefrontal regional cerebral glucose metabolism and greater depressive symptoms. However, the orbitofrontal regional cerebral glucose metabolism of patients with bulimia was not greater than that of comparison subjects, nor was higher orbitofrontal metabolism correlated with greater obsessive-compulsive disorder symptoms. **Conclusions:** These findings lead to the conclusion that left anterior lateral prefrontal cortex hypometabolism varies with the depressive symptoms observed in bulimia but that temporal lobe hypermetabolism and asymmetries appear to be independent of the mood state.*

(Am J Psychiatry 1992; 149:1506-1513)

Positron emission tomography (PET) with [^{18}F]-fluorodeoxyglucose (FDG) offers a method for examining the functional metabolic activity of brain regions. Our purpose in this study was to further delineate the character of cerebral metabolism in bulimia nervosa and to determine if functional links could be made between regional cerebral metabolism and the symptoms of depression, obsessive-compulsive disorder, and bulimia nervosa.

Bulimia nervosa is a psychiatric disorder characterized by rapid, uncontrolled, and compulsive ingestion of large quantities of food during discrete periods of time (binge eating), the regular use of extreme efforts to control weight (e.g., vomiting, laxative or diuretic abuse, vigorous exercise), and a persistent overconcern with body shape and weight (*DSM-III-R*). It is most commonly seen in young women.

The etiology of bulimia nervosa is unknown but may involve neurochemical, neuroendocrine, genetic, and psychosocial factors (1-3). Symptoms of major depression and obsessive-compulsive disorder often accompany bulimia nervosa. Because of this, clinicians have approached bulimia nervosa through treatment plans

that model the disorder as a mood disorder, as a personality disorder, as obsessive-compulsive disorder, or as a unique pathophysiological entity.

Wu et al. (4) and Hagman et al. (5) studied one set of PET data from a group of eight women with bulimia nervosa. These authors reported different patterns of hemispheric metabolism among three groups—normal volunteers, depressed patients, and patients with bulimia nervosa. Although patients with bulimia nervosa have a very high rate of depression and depressive symptoms (3), these authors did not find a metabolic correlation between bulimia nervosa and depression.

Bulimia nervosa is associated with major depression and obsessive-compulsive disorder, and both have been studied with FDG PET (6-10). Baxter et al. (6) found that lower regional cerebral metabolism of the left anterior lateral prefrontal cortex correlated significantly with greater severity of depressive symptoms. Lower metabolism of the right anterior lateral prefrontal cortex also correlated with greater depressive symptoms but less strongly.

Reduced activity of the left anterior lateral prefrontal cortex has also been implicated in depression secondary to stroke. Robinson and Starkstein (11) found that damage to the left anterior lateral prefrontal cortex correlated significantly with a higher incidence of major depressive episode. Damaged areas that were further from the left anterior lateral prefrontal cortex were less associated with depression than those closer to the left anterior frontal pole.

Baxter et al. (6) studied patients with obsessive-com-

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pulsive disorder who did or did not have concomitant major depression and found that left anterior lateral prefrontal cortex regional cerebral glucose metabolism varied with depressive symptoms but orbitofrontal hypermetabolism was present in patients in the absence of clinical depression. Nordahl et al. (7) and Baxter et al. (8) found that patients with obsessive-compulsive disorder had higher orbitofrontal metabolic rates.

Patients with bulimia nervosa experience perturbations of appetite and eating behavior, and these symptoms and signs often persist in the absence of depressed mood. Thus, certain regional cerebral glucose metabolism abnormalities in bulimia nervosa might be expected to be associated with depression but others might be independent of mood state and obsessiveness. One could then infer that these areas might be associated with the core eating behaviors of bulimia nervosa.

Patients with bulimia nervosa experience obsessive thoughts (regarding food and body weight and image) and have compulsive eating behaviors. It would therefore be interesting to see if there were a link between the clinical obsessive-compulsive disorder symptoms of bulimia nervosa and orbitofrontal metabolism. Such an examination was not reported by Wu et al. (4) or Hagman et al. (5).

METHOD

Subject Selection

Our 11 bulimic subjects were inpatients at the National Institutes of Health on a unit for eating disorders. Patients admitted to this study were initially screened to establish the diagnosis of bulimia nervosa by *DSM-III-R* criteria and to exclude medical illness, neurological illness, and histories of psychotic episodes, seizures, CNS infection, or loss of consciousness. All subjects chosen were women who were between 85% and 115% of their appropriate average body weight according to actuarial tables. All patients binged and vomited at least once a day. All patients gave written consent after information about radiation doses and procedures were explained fully.

The bulimic patients were evaluated for symptoms of obsessive-compulsive disorder and major depression with the Maudsley Obsessive-Compulsive Inventory (12) and the Hamilton Rating Scale for Depression.

For the first week, patients were allowed to live on the ward without the staff interfering with their eating behavior except for round-the-clock monitoring. Routine blood chemistries, ECGs, and physical examinations were conducted to assure that all patients were in no imminent physical danger if they continued this behavior. Patients consented to and were aware of being observed. Binge eating and purging frequency were documented in this fashion.

After the first week, patients entered a phase during which they were abstinent from binge eating and purging. During this phase patients received group and individual supportive psychotherapy and behavior modification but no psychotropic medications. This is the phase during

which PET scanning was performed. Each patient's caloric intake was closely monitored on a closed ward setting. The patients had been abstaining from binge eating and purging behaviors for at least 3 weeks but no more than 5 weeks when the PET scans were obtained. They maintained a constant (± 1 kg) normal body weight (85%–115% of the appropriate average).

Finally, the patients entered an open clinical phase during which they could make choices about receiving appropriate psychotropic medication and/or continuing psychotherapy. The average inpatient stay was 9 weeks.

The 18 nonpatient comparison subjects, who were normal volunteers, were matched with patients for age, sex, and educational level. Their mean age was 25.3 years ($SD=3.7$), compared with 25.5 ($SD=3.5$) for the patients, and their mean number of years of education was 15.6 ($SD=2.7$), compared with 14.2 ($SD=1.8$) for the patients. Comparison subjects were screened for a history of psychiatric, neurological, and medical illness. Results of physical examination and laboratory tests, including thyroid function tests, were within normal limits.

Scanning Procedure

All subjects were scanned 2–3 hours after a light meal. After information was provided and consent was given, intravenous and arterial lines were placed for tracer administration and serial blood sampling. If radial arterial line placement was unsuccessful, blood sampling was done from a second intravenous site that was "arterialized" with a local heating pad. Subjects were placed on the scanner table, and their heads were immobilized with a thermoplastic mask.

After aligning the PET camera to the canthomeatal line, a 7.5-minute transmission scan was performed for measured attenuation correction.

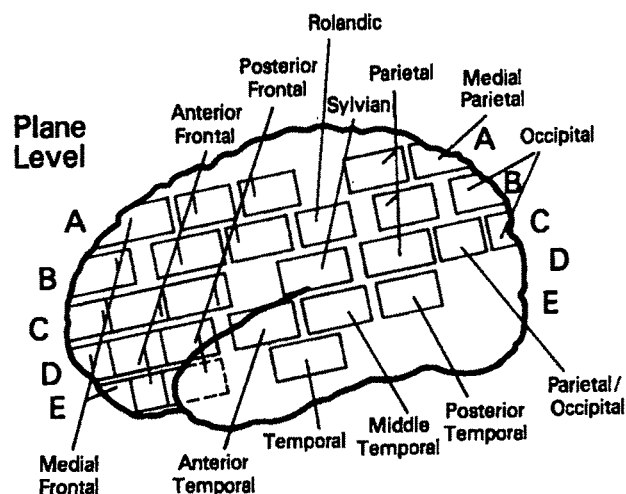
Subjects' eyes were covered and headphones were used while 5 mCi of FDG was administered and subjects performed a continuous discrimination task for 30 minutes (13). At the end of this 30-minute period, the headphones were removed and four scans of seven slices each were acquired over the next 30 minutes. During this time, serial blood samples were obtained so that a time-activity curve could be constructed and to verify that blood glucose was stable. The conversion of image pixel values from nanocuries per cubic centimeter micromoles of glucose per minute per 100 g tissue was performed by using methods described elsewhere (14–17).

Scanning was done on the Scanditronix PC1024-7B PET scanner. This scanner's in-plane resolution is 5.2 mm (resolution full width half maximum) at the center of the gantry. The axial resolution (slice thickness) is 10 mm at the center of the gantry, and the slice separation is 3.5 mm.

Data Analysis

The data were analyzed from both a hypothesis-driven approach and a systematic approach. Since previous studies have found correlations between depres-

FIGURE 1. Lateral View of Placement of Regions of Interest for PET Study



sive symptoms and activity in the left anterior lateral prefrontal cortex, differences in the orbitofrontal cortex between bulimic patients with obsessive-compulsive symptoms and comparison subjects, and differences in asymmetries in the temporal lobes between bulimic patients and comparison subjects, we used a univariate approach specifically to analyze differences in these regions. For the sake of completeness, the remainder of the cerebral regions are reported without correction for multiple comparisons.

To analyze the data in both a hypothesis-driven and a systematic manner, a template of 60 regions of interest was placed on PET slices by two independent raters who were not aware of the subjects' diagnoses. Slice selection and region placement, described elsewhere (13), were visually selected by the rater to match structures illustrated in the Matsui-Hirano atlas of the human brain (18). Figure 1 presents a lateral view of the placement of regions of interest.

Global cortical gray matter metabolic rates were calculated by finding the mean of the 49 cortical regions. Normalized regional cerebral glucose metabolic rates were calculated by dividing the regional cerebral metabolic rates by the global cortical gray matter metabolic rate (19).

Normalized regional cerebral glucose metabolism values of diagnostic groups were compared by using unpaired *t* tests and analysis of variance where appropriate. Nonmidline homologous hemispheric pairs of regions were compared by using paired *t* tests to evaluate for asymmetry. Scores from clinical rating scales, cognitive tests, and observed rates of binge eating and purging were correlated with regional cerebral glucose metabolism values by using linear regression. Two-tailed *t* tests were used unless otherwise indicated.

RESULTS

The patients with bulimia and the comparison subjects did not differ with respect to their global gray glu-

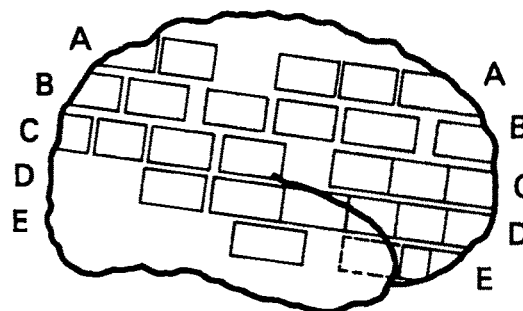
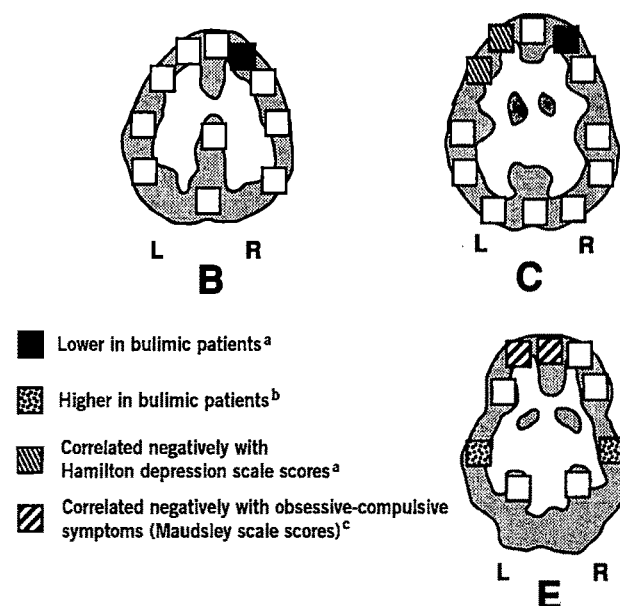


FIGURE 2. Regional Relative Cerebral Glucose Metabolic Rates in 11 Inpatients With Bulimia and 18 Normal Comparison Subjects



^a*p*<0.05.

^b*p*<0.01.

^c*p*<0.02.

cose metabolic rates (49.8 μ moles glucose/minute/100 g tissue, SD=8.8, versus 54.5 μ moles glucose/minute/100 g tissue, SD=9.4). Bulimic patients had significantly lower absolute glucose metabolism in the right anterior frontal region of plane B (49.01 μ mol/min/100 g tissue, SD=9.78) than comparison subjects (58.26 μ mol/min/100 g tissue, SD=11.18) (*t*=-2.27, *df*=27, *p*=0.03).

Figure 2 and tables 1 and 2 present normalized regional glucose metabolism values in the prefrontal and temporal cortex of the patients with bulimia and the comparison subjects. The patients with bulimia had sig-

TABLE 1. Normalized Regional Cerebral Glucose Metabolism Values in Planes A, B, C, D, and E for Inpatients With Bulimia and Normal Comparison Subjects

Region	Glucose Metabolism ($\mu\text{mol}/\text{min}$ per 100 g of tissue)				p	Change (%)
	Comparison Subjects (N=18)		Inpatients With Bulimia (N=11)			
	Mean	SD	Mean	SD		
A plane: 94 mm above canthomeatal line						
Anterior medial cortical	1.033	0.095	1.019	0.077	0.69	-1.4
Middle medial cortical	0.987	0.121	0.967	0.083	0.63	-2.0
Posterior medial cortical	1.101	0.167	1.139	0.119	0.52	3.6
Left anterior frontal	1.034	0.091	1.024	0.091	0.77	-1.0
Right anterior front	1.051	0.081	1.027	0.067	0.42	-2.3
Left posterior frontal	1.041	0.090	1.031	0.052	0.74	-1.0
Right posterior frontal	1.030	0.091	0.997	0.068	0.32	-3.2
Left parietal	1.061	0.085	1.068	0.081	0.84	0.7
Right parietal	1.081	0.094	1.073	0.079	0.83	-0.7
B plane: 81 mm above canthomeatal line						
Anterior medial cortical	1.051	0.072	1.018	0.116	0.36	-3.1
Superior occipital	1.127	0.122	1.095	0.134	0.52	-2.8
Left anterior frontal	1.052	0.071	1.047	0.098	0.87	-4.8
Right anterior frontal	1.069	0.085	0.983	0.095	0.02	-8.0 ^a
Left posterior frontal	1.087	0.136	1.097	0.098	0.83	0.9
Right posterior frontal	1.112	0.106	1.052	0.086	0.12	-5.4
Left Rolandic	0.969	0.089	0.944	0.085	0.46	-2.6
Right Rolandic	0.943	0.067	0.938	0.080	0.84	-0.5
Left parietal	0.992	0.063	1.018	0.092	0.36	2.6
Right parietal	1.014	0.064	0.983	0.093	0.30	-3.1
C plane: 67 mm above canthomeatal line						
Anterior medial frontal	0.999	0.076	0.984	0.071	0.60	-1.5
Occipital	0.999	0.091	0.990	0.174	0.86	-1.0
Left anterior frontal	1.032	0.093	0.093	0.985	0.07	-4.6
Right anterior frontal	1.066	0.090	0.997	0.083	0.04	-6.8 ^b
Left posterior frontal	1.086	0.070	1.058	0.094	0.38	-2.6
Right posterior frontal	1.106	0.080	1.058	0.081	0.15	-4.3
Left Sylvian	0.997	0.065	0.994	0.082	0.90	-0.3
Right Sylvian	0.987	0.055	0.954	0.071	0.17	-3.3
Left parietal	0.963	0.077	0.958	0.120	0.91	-0.5
Right parietal	0.959	0.084	0.927	0.069	0.31	-3.3
Left parietal occipital	0.815	0.075	0.851	0.091	0.25	4.4
Right parietal occipital	0.807	0.081	0.857	0.096	0.14	6.2
D plane: 53 mm above canthomeatal line						
Anterior medial frontal	0.991	0.060	0.998	0.108	0.82	0.7
Left anterior frontal	1.060	0.057	1.042	0.079	0.48	-1.7
Right anterior frontal	1.070	0.042	1.059	0.119	0.71	-1.0
Left posterior frontal	1.015	0.063	1.041	0.122	0.77	2.6
Right posterior frontal	0.993	0.066	0.994	0.090	0.09	0.1
Left anterior temporal	1.607	0.074	1.020	0.088	0.66	1.3
Right anterior temporal	1.015	0.081	1.041	0.113	0.47	2.6
Left middle temporal	0.980	0.074	1.037	0.087	0.07	5.8
Right middle temporal	0.971	0.080	1.003	0.075	0.29	3.3
Left posterior temporal	0.863	0.081	0.915	0.090	0.13	6.0
Right posterior temporal	0.817	0.075	0.873	0.065	0.07	6.9
E plane: 40 mm above canthomeatal line						
Anterior medial frontal	0.949	0.092	0.972	0.061	0.47	2.4
Left anterior frontal	0.972	0.111	0.986	0.071	0.71	1.4
Right anterior frontal	0.997	0.106	1.004	0.083	0.86	0.7
Left posterior frontal	0.961	0.077	0.992	0.080	0.31	3.2
Right posterior frontal	0.967	0.088	1.017	0.076	0.13	5.2
Left temporal	0.868	0.062	0.938	0.059	0.01	8.1 ^c
Right temporal	0.855	0.047	0.936	0.094	0.005	9.5 ^d
Left hippocampal	0.712	0.068	0.760	0.061	0.07	6.7
Right hippocampal	0.707	0.072	0.743	0.044	0.10	5.8

^at=-2.53, df=27, p=0.02.^bt=2.13, df=27, p=0.04.^ct=2.97, df=27, p=0.006.^dt=3.06, df=27, p=0.005.

nificantly lower values than comparison subjects in plane B in the right anterior prefrontal region and in plane C in the right anterior prefrontal region (table 1). Bulimic patients also had significantly higher values

than comparison subjects bilaterally in plane E in the temporal regions (table 1).

The two groups performed the continuous discrimination task comparably. The patients had a mean of

TABLE 2. Normalized Regional Cerebral Glucose Metabolism Values in Subcortical Regions for Inpatients With Bulimia and Normal Comparison Subjects

Region	Glucose Metabolism (μmol/min per 100 g of tissue)				p	Change (%)
	Comparison Subjects (N=18)		Inpatients With Bulimia (N=11)			
	Mean	SD	Mean	SD		
Cingulate	1.057	0.121	1.012	0.114	0.32	-4.3
Left caudate	1.042	0.107	0.996	0.119	0.29	-4.4
Right caudate	0.991	0.102	1.022	0.133	0.49	3.1
Left anterior putamen	1.014	0.119	1.060	0.130	0.34	4.5
Right anterior putamen	1.014	0.111	1.009	0.178	0.93	-0.5
Left posterior putamen	0.955	0.122	1.003	0.140	0.97	5.0
Right posterior putamen	0.919	0.093	0.914	0.152	0.91	-0.5
Left thalamus	0.953	0.129	1.025	0.083	0.11	7.6
Right thalamus	0.948	0.126	1.034	0.103	0.07	9.1

TABLE 3. Regional Asymmetry in Inpatients With Bulimia and Normal Comparison Subjects

Group and Plane	Region	Mean Difference in Normalized Regional Cerebral Glucose Metabolism ^a	t	df	p
Inpatients with bulimia					
A	Posterior frontal	Left 0.033 greater than right	2.31	10	0.04
B	Anterior frontal	Left 0.064 greater than right	3.42	10	0.007
D	Posterior putamen	Left 0.089 greater than right	3.73	10	0.004
D	Parietal temporal	Left 0.042 greater than right	4.44	10	0.001
D	Middle temporal	Left 0.035 greater than right	2.25	10	0.05
Comparison subjects					
D	Caudate	Left 0.052 greater than right	2.32	17	0.03
C	Anterior frontal	Right 0.034 greater than left	-2.90	17	0.01
D	Parietal temporal	Left 0.047 greater than right	2.98	17	0.008

^aValues are micromoles of glucose per minute per 100 g of tissue.

164.1 correct identifications (SD=55.4), and the comparison subjects had a mean of 187.7 (SD=29.5). The patients had a mean of 4.1 false alarms (SD=4.2), and the comparison subjects had a mean of 10.1 (SD=14.1).

Nonmidline regions were analyzed for asymmetry to compare our results from this group of subjects with those of Wu et al. (4). Table 3 summarizes these results. Asymmetry of glucose metabolism was found in the comparison group in plane C in the anterior prefrontal regions and in plane D in the parietal temporal regions and the caudate (table 3). The prefrontal and caudate asymmetries found in the comparison subjects were not found in the bulimic patients, but the plane D parietal temporal asymmetry was present (table 3). Additional asymmetries were found in bulimic patients in plane B in the anterior frontal regions, in plane A in the posterior frontal regions, and in plane D in the middle temporal region and the posterior putamen (table 3).

There were only three hemispheric pairs that statistically differed between groups. Patients with bulimia had greater left-sided than right-sided activity than comparison subjects in plane B in the anterior frontal regions ($t=3.21$, $df=27$, $p=0.003$) and parietal regions ($t=2.30$, $df=27$, $p=0.03$). Patients with bulimia also had greater right-sided than left-sided activity than comparison subjects in plane D in the caudate ($t=-2.12$, $df=27$, $p=0.04$).

The regional cerebral glucose metabolism in the plane E orbitofrontal regions of bulimic patients was compared with that of comparison subjects and correlated with the patients' scores on the Maudsley Obsessive-Compulsive Inventory. The patients with bulimia nervosa did not have higher orbitofrontal metabolism than the comparison subjects, nor did their metabolism in these regions correlate positively with their scores on the Maudsley Obsessive-Compulsive Inventory. Two of the orbitofrontal regions in bulimic patients correlated negatively with higher Maudsley scores (anterior medial, $F=8.12$, $r^2=0.47$, $df=10$, $p=0.02$; left anterior, $F=9.23$, $r^2=0.51$, $df=10$, $p=0.01$). There were nonsignificant trends toward negative correlations with higher Maudsley scores in the other three orbitofrontal regions.

Correlations between prefrontal and temporal areas and Hamilton depression scale scores in the bulimic patients were tested by using simple regression. In plane C, the left anterior ($F=4.99$, $r^2=0.38$, $df=9$, $p=0.03$, one-tailed t test) and the left posterior ($F=5.92$, $r^2=0.42$, $df=9$, $p=0.02$, one-tailed t test) prefrontal regional glucose metabolism correlated negatively with higher Hamilton depression scale scores. There was a trend toward negative correlation with higher Hamilton depression scale scores in plane C in the right anterior prefrontal region ($F=3.02$, $r^2=0.27$, $df=9$, $p=0.06$,

one-tailed *t* test) (figure 3), but other prefrontal and temporal regions were not significantly correlated with the Hamilton depression scale scores. When the patients whose Hamilton depression scale scores were 15 or greater (18 comparison subjects and seven patients with bulimia) were considered separately, mean regional cerebral glucose metabolism values in the left anterior and posterior lateral prefrontal cortex were significantly lower than those of comparison subjects ($t=-1.96$, $df=23$, $p=0.03$, and $t=-1.83$, $df=23$, $p=0.04$, respectively, one-tailed *t* test).

At the time of the PET scan, these bulimic patients had abstained from binge eating and purging for at least 3 weeks but not more than 5 weeks. Neither the frequency of their pre-abstinence binge eating nor their caloric intake correlated with prefrontal or temporal metabolism. The frequency of binge eating episodes did correlate positively with higher metabolism bilaterally in the posterior frontal area of plane A and in the right parietal area of plane A. These areas were not considered in any a priori hypothesis and were not significant after correction for multiple comparisons.

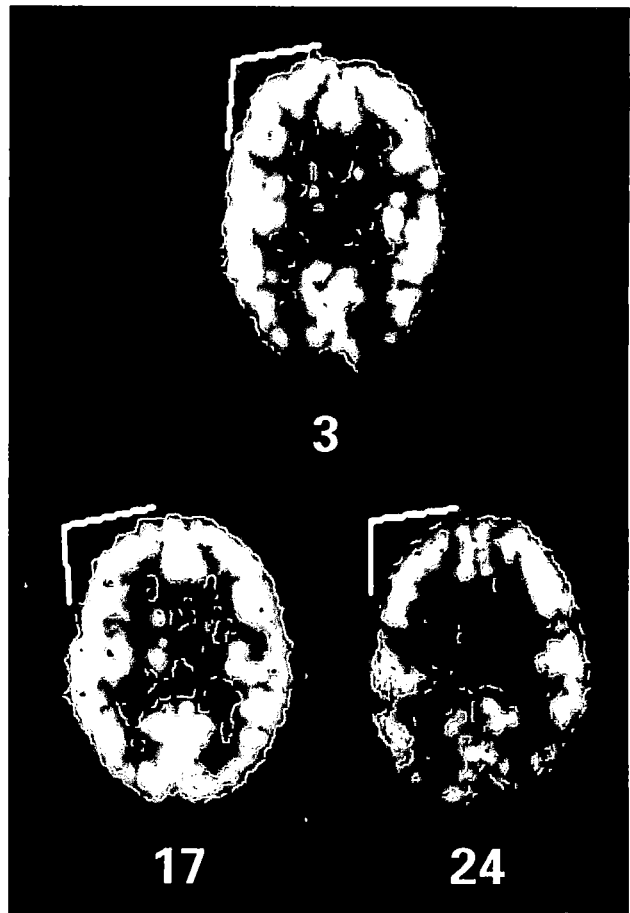
CONCLUSIONS AND DISCUSSION

This study presents a controlled and systematic view of a complex clinical syndrome. Great care was taken to assure that regional differences and correlations were not influenced by metabolic factors due to electrolyte imbalance, starvation states, or lack of homogeneity due to binge eating and purging. At this point we would like to comment on two issues with regard to data analysis: statistical interpretation of multiple comparisons and localization of anatomical structures on the PET image.

With regard to the analysis of multiple regions, a template of 60 regions was used to standardize the blind rating process and our approach to the examination of PET images. Regions selected for statistical comparisons in this work were divided into two groups: 1) regions based on a priori hypotheses formed from metabolic asymmetry, clinical correlations, and mean regional metabolic differences found in other work (4–8, 11) and 2) other regions reported for the benefit of the reader. We did not correct for multiple comparisons in the analysis of regions for which we had a priori hypotheses because this would be statistically unwarranted and overly magnify the possibility of making type II errors. Other regions were analyzed on an exploratory basis and probability values were reported without corrections for multiple comparisons so that the reader might judge their possible significance or lack thereof. This type of statistical treatment is consistent with several articles (6, 7, 10, 13).

Localization of anatomic structures was accomplished by using the Matsui-Hirano atlas of the human brain (18). This method has proven reliable as used by our group. Using this method we have been able to replicate the findings of hypermetabolism in the orbitofrontal lobes in pa-

FIGURE 3. PET Images of C-Plane Slice of Left Anterolateral Prefrontal Cortex of Three Bulimic Inpatients With Different Hamilton Depression Scale Scores^a



^aThe numbers indicate the patients' Hamilton depression scale scores.

tients with obsessive-compulsive disorder and hypometabolism in the left anterolateral prefrontal cortex in depression reported by Baxter et al. (6, 8) and Nordahl et al. (7). There are other methods of anatomic localization that use computer fitting of magnetic resonance imaging (MRI) or computed tomography (CT) scans. These systems were not available to us at the time this data set was acquired, and MRI scans of the quality necessary for coregistration were not done.

We did not find differences between the global (gray) metabolic rates of patients with bulimia nervosa and normal comparison subjects. Consistent with the findings of Wu et al. (4), we observed a multiple regional, left-greater-than-right hemispheric asymmetry in the temporal lobes of patients with bulimia that was not observed in comparison subjects. Also consistent with the findings of Wu et al. we observed a right-greater-than-left frontal hemispheric asymmetry in the comparison group that was not present in the bulimic patients. In addition to the temporal lobe hemispheric asymmetries, we observed relative bilateral inferior temporal lobe hypermetabolism.

Orbitofrontal regions were analyzed to compare the results for our group of bulimic patients with those for patients with obsessive-compulsive disorder studied by Nordahl et al. (7) and Baxter et al. (8). There was no difference in mean regional cerebral glucose metabolism, nor was there a positive correlation between regional cerebral glucose metabolism and obsessive-compulsive disorder symptoms (according to the Maudsley Obsessive-Compulsive Inventory) in the orbitofrontal regions. Conversely, there were negative correlations between obsessive-compulsive disorder symptoms and orbitofrontal metabolism in the medial and left lateral orbitofrontal regions and a trend toward a negative correlation in the right lateral orbitofrontal region. This might lead one to believe that orbitofrontal regions may subserve more than one function. For example, although bulimic patients have obsessive thoughts, disinhibited eating behavior may be connected with lower orbitofrontal metabolism. This might effectively hide orbitofrontal increases connected with obsessive thoughts. Alternatively, orbitofrontal regions could be a biological determinant for impulse control rather than being responsible for the generation of obsessive thoughts (20).

A study of anorectic patients who have obsessive thoughts about food but do not impulsively binge might find elevated orbitofrontal regional cerebral glucose metabolism like that of patients with obsessive-compulsive disorder. This type of study was performed by Herholz et al. (21), but they did not report higher orbitofrontal metabolism; the orbitofrontal area was not analyzed distinctly from the prefrontal or frontal areas. If the orbitofrontal area were analyzed distinctly, this hypothesis could be more reasonably tested.

In addition to confirming the findings of Wu et al. (4) and Hagman et al. (5), we found regional mean hypermetabolism bilaterally in the inferior temporal lobes and hypometabolism in the right anterior lateral prefrontal cortical areas. Design and implementation differences between our study and that of Wu et al. and Hagman et al. may be responsible for the different regional metabolic findings. First, we scanned nearly twice the number of subjects (they scanned eight comparison subjects and eight bulimic subjects), which increases the statistical power of finding smaller but significant mean differences. Second, the scanner used in our study had a slightly finer resolution (5.2 mm versus 7.6 mm in plane, resolution full width half maximum). Finally, we believe that the empirical attenuation correction increases the validity of our orbitofrontal values. Orbitofrontal metabolic values are difficult to measure with a calculated attenuation correction due to the variable bone density in the skull. Empirically measuring the attenuation correction decreases the variability of the observed orbitofrontal metabolic rates by measuring and correcting for the individual bone density.

Although we did not observe a pattern characteristic of obsessive-compulsive disorder in our bulimic patients, we did observe patterns typical of depressed patients. Metabolism in left anterior and posterior lateral prefrontal cortical areas correlated negatively with

Hamilton depression scale scores. When the patients whose Hamilton depression scale scores were 15 or greater were considered separately, mean regional cerebral glucose metabolism values in the left anterior and posterior lateral prefrontal cortex were found to be significantly lower than those of comparison subjects. This is consistent with and adds another diagnostic group to the regional cerebral glucose metabolism findings of Baxter et al. (6) in their study of depression in affective disorders and obsessive-compulsive disorder.

Hagman et al. (5) reanalyzed the data from eight bulimic women that Wu et al. (4) collected and compared them with scans of eight age-matched depressed women. They did not observe lower mean metabolism in the right or left anterior lateral prefrontal cortex in either depressed or bulimic subjects than in a group of comparison subjects. They did not report correlations between these subjects' Hamilton depression scale scores and their left anterior lateral prefrontal cortex regional cerebral glucose metabolism. Due to the lower numbers of subjects per cell, compared with the data of Baxter et al. (6) and this study, we believe there was not enough statistical power in the study of Wu et al. (4) and Hagman et al. (5).

The patients in our study were inpatients whose eating behavior was closely controlled. At the time of the PET scan these patients had abstained from binge eating and purging for at least 3 weeks but not more than 5 weeks. Neither the frequency of their pre-abstinence binge eating nor their caloric intake correlated with prefrontal or temporal metabolism. The frequency of binge eating episodes did correlate positively with higher metabolism bilaterally in the posterior frontal area of plane A and in the right parietal area of plane A; however, none of these areas was found in the similar correlations of Hagman et al. (5). Likewise, none of the correlations of frequency of binge eating found in the study of Hagman et al. was observed in this study group. One might therefore infer that if there is a correlation between binge eating frequency and regional cerebral glucose metabolism, it is a state-dependent correlation, or one might infer that the correlations observed occurred simply by chance because we had no a priori hypothesis for this particular region.

Hagman et al. (5) suggested a study that might include patients with bulimia with varying degrees of mood disturbance in order to elucidate the significance of mood disturbance within the syndrome. Our study satisfies this request and leads one to believe that left anterior lateral prefrontal cortex hypometabolism varies with the depressive symptoms observed in bulimia but that temporal lobe hypermetabolism and asymmetries appear to be independent of the mood state.

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Coping With the Threat of AIDS: The Role of Social Support

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Objective: There has been relatively little clinical research on how asymptomatic HIV-positive men cope with the threat of AIDS. The present study was intended to 1) describe the coping strategies used by asymptomatic HIV-positive homosexual men, 2) examine the relationship of coping to dysphoria and self-esteem, and 3) explore how race and social support correlate with coping. **Method:** The study group was composed of 52 asymptomatic HIV-positive homosexual men. A group of 53 HIV-negative homosexual men was used for descriptive comparison. Data on coping, social support, dysphoria, and self-esteem came from self-report measures; depression was also determined by interviews with the Hamilton Rating Scale for Depression. **Results:** The authors found that 1) subjects primarily coped with the threat of AIDS by adopting a fighting spirit, reframing stress to maximize personal growth, planning a course of action, and seeking social support; 2) more helpless coping, less fighting spirit, and less personal growth were related to dysphoria and poor self-esteem, whereas denial was related to more depression, anger, and helpless coping; 3) satisfaction with one's social support networks and participation in the AIDS community were related to more healthy coping strategies (e.g., fighting spirit, personal growth); and 4) black subjects expressed more denial, more helplessness, and less social support. **Conclusions:** These results suggest that health professionals should encourage more adaptive coping strategies, help patients use existing sources of positive social support, and assist patients, particularly black patients, in finding community support networks.

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Infection with HIV raises a wide spectrum of concerns and fears among infected individuals. Even before symptoms occur, those infected with HIV have concerns about future economic security; sexuality and disease transmission; rejection from family, friends, and lovers; and eventual ill health and death. Previous research has focused on psychiatric alterations associated with HIV-positive status, most notably depression and anxiety (1-5). The present study focused on how asymptomatic HIV-positive homosexual men cope with the threat of AIDS. Among seropositive men, we 1) examined the relationship of coping to dysphoria and self-esteem in order to determine the positive or negative aspects of various coping strategies and 2) explored how social support and race are related to cop-

ing. We also studied the coping strategies (e.g., fighting spirit, helplessness, denial) used by HIV-positive men and compared these strategies with those of seronegative comparison subjects.

Much has been written about the role of coping in buffering the psychological impact of stress and possibly altering the progression of disease (e.g., cancer, AIDS). In cancer patients, Greer et al. (6) found that fighting spirit and denial were associated with a better prognosis than was helplessness or stoicism. Regardless of whether coping has a direct role in HIV disease outcome, it may have an important role in preventing depression as the threat of AIDS becomes a reality for those who were previously asymptomatic. The following questions remain: 1) Which coping strategies indicate the most healthy adaptive pattern? and 2) What role does social support play in eliciting adaptive coping styles?

Coping generally refers to "the cognitive and behavioral efforts to manage specific external and/or internal demands appraised as taxing or exceeding the resources of the individual" (7). To our knowledge, however, there has been no agreement on or exhaustive list of cognitive and behavioral efforts or strategies that people use to deal with threats. Although it has been assumed that active strategies are good and that passive

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strategies are bad, only a few studies have delineated the mental health correlates of a variety of coping styles in people with HIV infection. Among homosexual men coping with HIV-related illness, two studies (8, 9) showed that active-behavioral coping was associated with enhanced mood and self-esteem and that avoidance coping (denial) was related to greater total mood disturbance and lower self-esteem. One study (5) showed no significant association between active or avoidant coping and psychological distress. In cancer patients, passive and suppressive coping strategies were related to emotional distress, whereas active coping styles (e.g., confronting problems, sharing concerns) were associated with less dysphoria (10). Our determination of adaptive or healthy coping strategies has been based on the relationship of the coping measures to depression, tension, anger, and self-esteem.

Given that more active coping strategies indicate better adaptation, what is the evidence that social support may lead to more adaptive coping styles? Among HIV-infected homosexual men, social support was shown to correlate positively with active coping and negatively with avoidance (8, 9). Other studies of HIV-infected men have shown a clear relationship of social support to less mood disturbance (5, 11–14), less helplessness (14), and greater self-esteem (12). In addition, social support has been linked to less anxiety and depression in a variety of community samples (15, 16).

In the present study we extended the work of others by looking at the relationship of seven specific coping styles to several measures of dysphoria, self-esteem, and social support. We hypothesized that coping by maintaining a fighting spirit, planning, personal growth, and seeking social support would be related to positive affect and self-esteem, whereas denial and helpless coping would be associated with negative affect and self-esteem. Furthermore, we hypothesized that social support, as measured by a variety of indicators (e.g., support satisfaction, participation in the AIDS community), would be associated with more fighting spirit, planning, personal growth, seeking social support, and religious coping and with less helplessness and denial. In addition to these hypotheses, we explored possible race differences in social support and coping. Furthermore, to describe the seropositive men, we compared their coping strategies to those of seronegative comparison subjects, since the threat of AIDS is inherently more immediate for those infected with HIV.

METHOD

Subjects

We studied 105 homosexual volunteers: 52 asymptomatic HIV-positive men and a comparison group of 53 HIV-negative men. This group is part of the Coping in Health and Illness Project, a large, multidisciplinary, longitudinal study. The study was approved by our institutional committee for the protection of human

rights, and all subjects provided written informed consent. Subjects were recruited from North Carolina county health departments and through homosexual organizations, advertisements, and word of mouth.

The men were between the ages of 18 and 50 years and were required to have at least a 10th-grade education or a general equivalency diploma and to have spoken English as their primary language before the age of 12. All HIV-positive subjects were asymptomatic, without AIDS or AIDS-related complex (e.g., night sweats, herpes zoster, oral candidiasis, hairy leukoplakia, shingles, unexplained fever or diarrhea, and unexplained weight loss or fatigue in the presence of other symptoms) according to the Centers for Disease Control criteria. All subjects were further screened to exclude any individual with important medical illness, a recent operation, or a history of intravenous drug use as a risk factor for HIV exposure. These screening criteria were included for the neuropsychological and psychoimmune aspects of the larger study.

Procedure

Over 2 nights and days at an inpatient research center, the subjects underwent psychiatric, physical, neurologic, and neuropsychological examinations and several blood samples. On the first evening, before any testing, each subject completed a packet of self-report questions about coping.

Measures

Coping was assessed by means of the Coping in Health and Illness Project questionnaire with a modification of the COPE (17). The subjects were asked to indicate on a 4-point scale ("not at all" to "very much") how they "generally cope with, or handle the threat of getting AIDS." The subjects indicated their coping responses to items included in five of the 14 scales of the COPE: 1) planning (e.g., "I try to come up with a strategy about what to do"), 2) positive reinterpretation and personal growth (e.g., "I try to see it in a different light, to make it seem more positive"), 3) seeking emotional social support (e.g., "I try to get emotional support from friends or relatives"), 4) denial (e.g., "I pretend that it hasn't really happened"), and 5) turning to religion (e.g., "I seek God's help"). In addition, we added items to create two additional scales, helpless coping and fighting spirit. Items for these two coping measures were modified versions of items from Greer and Watson's coping questionnaire for cancer patients (18). To create indexes of helpless coping and fighting spirit, we ran a principal factor analysis with quartimax rotation for each index; quartimax was used because we wanted to find the factor structure of a set of items. Initially, 11 fighting spirit items and nine helpless coping items were analyzed (for both the 52 HIV-positive and the 53 HIV-negative homosexual men). Items loading (greater than 0.38) on the primary factor were retained, yielding nine fighting spirit items and eight helpless coping items.

TABLE 1. Intercorrelations of Scores on Coping Scales for 52 HIV-Positive Homosexual Men

Coping Scale	Correlation (r) ^a						
	Helpless Coping	Denial	Fighting Spirit	Personal Growth	Planning	Seeking Social Support	Turning to Religion
Helpless coping	0.77	0.48 ^b	-0.32 ^c	-0.25	-0.35 ^b	-0.20	-0.02
Denial		0.82	-0.00	0.06	-0.13	-0.11	0.18
Fighting spirit			0.80	0.65 ^b	0.60 ^b	0.34 ^c	0.34 ^c
Personal growth				0.83	0.42 ^b	0.56 ^b	0.41 ^b
Planning					0.88	0.41 ^b	0.11
Seeking social support						0.82	0.15
Turning to religion							0.93

^aCronbach's alpha shown on diagonal.^bp<0.01, two-tailed; df=50.^cp<0.05, two-tailed; df=50.TABLE 2. Scores on Coping Scales for HIV-Positive and HIV-Negative Homosexual Men^a

Coping Scale	Score ^a				ANOVA ^b	
	HIV-Positive Men (N=52)		HIV-Negative Men (N=53)			
	Mean	SD	Mean	SD	F	p
Helpless coping	1.56	0.46	1.35	0.45	5.17	0.03
Denial	1.57	0.61	1.27	0.61	5.96	0.02
Fighting spirit	3.40	0.55	3.15	0.55	5.20	0.02
Personal growth	3.09	0.73	2.96	0.73	0.78	0.38
Planning	3.07	0.80	2.86	0.80	1.64	0.20
Seeking social support	2.86	0.80	2.91	0.81	0.08	0.78
Turning to religion	2.64	1.02	2.37	1.01	1.76	0.19

^aAdjusted mean scores are from analysis of covariance with race and education controlled. Range of possible scores is 1 to 4.^bTwo-tailed p values; df=1, 101.

Cronbach's alphas for both the HIV-positive and HIV-negative men were checked to ensure reliability of the scales for both groups. The item scores were summed and divided by the number of items to create all coping indexes, which ranged from 1 to 4. Table 1 shows the intercorrelations among coping indexes and the substantial Cronbach's reliability coefficients on the diagonal of the matrix (ranging from 0.77 to 0.93).

Depression and dysphoric mood for the past week were assessed with the self-report Carroll Rating Scale for Depression (19), the Profile of Mood States (POMS) (20), and the interview-based Hamilton Rating Scale for Depression (21). Consensus psychiatric diagnoses were made by reviewing a structured diagnostic interview (modified Structured Clinical Interview for DSM-III-R) (22, 23) at a diagnostic conference. The Rosenberg Self-Esteem Scale (24), a 10-item evaluation of the subject's self-esteem, was also administered.

We assessed social support in several ways. The Sarason Brief Social Support Questionnaire (25) assessed the degree of satisfaction with people the subject counted on for social support or help (Cronbach's alpha=0.86). Social conflict was measured with a seven-item inventory used in the Multicenter AIDS Cohort

Study (unpublished 1989 paper by K. O'Brien et al.) in its coping and change survey. The social conflict scale (Cronbach's alpha=0.87) addresses the degree of conflict the individual has experienced in the past month with the people in his personal life (e.g., "Have you felt irritated or resentful toward people in your personal life?"). We also developed a six-item scale to measure participation in the AIDS community (e.g., belonging to AIDS support groups and organizations, socializing with HIV-positive people) (Cronbach's alpha=0.75).

Statistical Methods

To describe the coping strategies of the study group, we first compared the seropositive and seronegative subjects on the seven coping variables by using multivariate analysis of variance (MANOVA). Significant results from MANOVA (Wilks's lambda, $F=3.79$, $df=7$, 97 , $p=0.001$) allowed us to perform separate analyses of covariance on the coping measures, with serostatus as the independent variable and education and race as covariates (table 2). Education and race were controlled, since these variables were correlated significantly with both serostatus and coping. The assumption of parallel regression of the covariates was met. The probability values in table 2 are two-tailed.

The remaining analyses were performed only for the HIV-positive subjects. Pearson product-moment correlation (with two-tailed significance tests) was used to show the interrelationships among the coping measures (table 1). Principal factor analysis with varimax rotation was used to confirm the pattern of correlation among the coping indexes (with 0.38 as the cut-off for inclusion in a factor). Cronbach's alpha for each coping index indicates the reliability or internal consistency of each measure.

To examine the relationship between coping and measures of dysphoria, we performed multiple regression analyses with the dysphoria measures as the dependent variables and the coping variables run separately as independent variables, holding constant age, education, race, and months since the subject learned he was HIV positive. These background variables were chosen because they were significantly related to some

TABLE 3. Partial Correlations Between Scores on Coping and Dysphoria Scales for 52 HIV-Positive Homosexual Men^a

Coping Scale	Partial Correlation With Dysphoria Scale (race controlled) (r)					Rosenberg Self-Esteem Scale
	Carroll Depression Scale	Hamilton Depression Scale	Profile of Mood States			
			Depression	Tension	Anger	
Helpless coping	0.47 ^b	0.39 ^b	0.37 ^b	0.28 ^c	0.12	-0.40 ^b
Denial	0.26 ^c	0.28 ^c	0.28 ^c	0.30 ^c	0.41 ^b	-0.10
Fighting spirit	-0.33 ^b	-0.28 ^c	-0.25 ^c	-0.24 ^c	-0.13	0.51 ^b
Personal growth	-0.29 ^c	-0.26 ^c	0.00	-0.15	0.08	0.33 ^b
Planning	-0.05	-0.02	-0.04	-0.06	-0.11	0.28 ^c
Seeking social support	-0.16	-0.11	0.07	-0.02	-0.14	0.18
Turning to religion	0.05	0.12	0.18	-0.09	0.00	-0.07

^aBecause of missing data, N=49 for the Hamilton scale and N=51 for the POMS indexes. In the statistical analyses, df=49 (Carroll and Rosenberg scales), df=46 (Hamilton scale), or df=48 (POMS).

^bp<0.01, one-tailed test.

^cp<0.05, one-tailed test.

of the coping measures. They were controlled to rule out the possibility of spurious findings. Only race altered the relationships of some coping measures to dysphoria (regression coefficient change of 20% or more). Therefore, table 3 shows the partial correlations of coping with depression, tension, anger, and self-esteem, with race controlled. All tests are one-tailed.

We were next interested in testing the relationship of coping to social support variables: support satisfaction, participation in AIDS groups, and social conflict. Since only race (and not age, education, or time since the subject learned he was seropositive) was related to social support and coping variables, we determined partial correlations between support and coping variables, holding race constant. Since a few of the zero-order relationships were diminished when we controlled for race, the results of the partial correlation analysis are shown in table 4. All tests are one-tailed because of the testing of directional hypotheses. We will also report the zero-order correlation coefficients (two-tailed) for the correlations of race with the coping and social support variables, as well as partial correlations of race and coping when social support is held constant.

RESULTS

The HIV-positive subjects had a mean age of 30.0 years (SD=6.7) and an average education of 14.4 years (SD=2.5), and 76.9% (N=40) were white. The HIV-negative subjects had a mean age of 30.9 years (SD=6.9) and an average education of 15.9 years (SD=2.4), and 90.6% (N=48) were white. Since we were interested in race effects on psychosocial variables, we compared the background characteristics of the black and white seropositive subjects. Although the differences were not significant, the blacks had less education (mean=13.3 years, SD=1.9) than the whites (mean=14.7, SD=2.6) ($t=1.74$, $df=50$, $p=0.09$), and the blacks were younger (mean age=27.8 years, SD=3.9) than the whites (mean=30.7, SD=7.2) ($t=1.8$, $df=34$, $p=0.08$). Only two (16.7%) of the blacks met the DSM-III-R criteria for

TABLE 4. Partial Correlations Between Scores on Coping Scales and Social Support Measures for 51 HIV-Positive Homosexual Men

Coping Scale	Partial Correlation With Support Measure (race controlled)			
	Satisfaction With Support ^a		Participation in AIDS Groups ^b	
	r	p ^c	r	p ^c
Helpless coping	-0.34	0.008	-0.13	0.19
Denial	-0.02	0.45	-0.02	0.43
Fighting spirit	0.35	0.006	0.11	0.22
Personal growth	0.46	0.0004	0.32	0.01
Planning	0.06	0.35	0.08	0.30
Seeking social support	0.52	0.0001	0.33	0.01
Turning to religion	0.36	0.005	0.14	0.16

^aScore on Sarason Brief Social Support Questionnaire.

^bRating on six-item measure.

^cOne-tailed test; $df=48$.

lifetime drug dependence or drug abuse, compared to 19 (47.5%) of the whites ($\chi^2=3.65$, $df=1$, $p=0.06$).

Table 2 shows the means (adjusted for race and education) and standard deviations for the ratings of coping measures for the seropositive and seronegative subjects. Most subjects endorsed fighting spirit, personal growth, planning, and seeking social support and rejected helpless coping and denial. The seropositive subjects generally coped with the threat of AIDS with more fighting spirit, yet also more denial and helplessness, than did the seronegative comparison subjects.

Table 1 shows the pattern of intercorrelation among the coping measures in the HIV-positive subjects. Factor analyses of these scales confirmed the two-factor pattern of correlation shown in table 1 (two factors with eigenvalues above 1). The first factor (explaining 69% of the variance in the matrix) included fighting spirit, personal growth, active planning, seeking emotional social support, and, to a lesser extent, religious coping. These five indexes might represent more active or positive coping strategies. The second factor (explaining 31% of the variance in the matrix) included helpless coping and denial. Thus, subjects who felt helpless when confronting the threat of AIDS also tended to deny this threat ($r=0.48$,

$df=50$, $p=0.0004$). Denial and helplessness may represent more passive or negative coping responses.

Our next question was whether particular coping strategies were related to positive or negative affect (dysphoria) or to self-esteem. Overall the seropositive subjects scored relatively low on our depression measures (Hamilton Rating Scale for Depression: mean=4.69, $SD=4.79$; Carroll Rating Scale for Depression: mean=9.13, $SD=6.76$). Only five (9.6%) met the *DSM-III-R* criteria for a current major depression, although fully 21 (40.4%) had had major depression during their lifetimes. Table 3 shows the partial correlations of coping with depression, tension, anger, and self-esteem when race was controlled (race was the only covariate that altered the relationships of coping to dysphoria and self-esteem). The homosexual men who felt helpless about the threat of AIDS were significantly more depressed and tense and had lower self-esteem. Denial was also consistently associated with dysphoric states, particularly angry mood. The subjects with fighting spirit tended to be less depressed on all measures and had much higher self-esteem. Reacting to the AIDS threat by seeing it as an opportunity for personal growth was also significantly associated with less depression and with more self-esteem. Having plans to cope with the threat of AIDS was unrelated to all dysphoria measures, although it was related to better self-esteem. Finally, coping by seeking social support or by turning to religion was not significantly correlated with the dysphoria measures or with self-esteem.

Before analyzing the relationship between social support and coping, we were interested in whether there were race differences on the coping and social support measures. Blacks were more likely than whites to endorse the coping strategies of helplessness ($r=0.29$, $df=50$, $p=0.04$), denial ($r=0.33$, $df=50$, $p=0.02$), and turning to religion ($r=0.32$, $df=50$, $p=0.02$) and were less likely to seek emotional support ($r=-0.42$, $df=50$, $p=0.002$) to cope with AIDS. These race differences were not explained by age, education, or time since the subject learned of his serostatus. The races did not differ on the other coping indexes. Blacks' greater dissatisfaction with existing social support networks ($r=-0.28$, $df=50$, $p=0.05$) largely explained their greater feelings of helplessness (partial $r=0.13$, $df=49$, $p=0.36$) and somewhat explained their lower tendency to seek emotional support (partial $r=-0.29$, $df=49$, $p=0.04$).

Table 4 shows the relationship between social support measures and coping strategies when race was held constant. Satisfaction with support contributed to significantly less helpless coping, more fighting spirit, more personal growth, greater likelihood of seeking social support to deal with AIDS, and more turning to religion for help. Furthermore, participation in the AIDS community was associated with significantly more personal growth and a significantly greater tendency to seek emotional support as a way of coping with AIDS. Conflict in social relationships was unrelated to coping except that the subjects with more conflict were significantly less likely to seek social sup-

port when threatened by AIDS (partial $r=-0.33$, $df=49$, $p=0.02$).

Planning was unrelated to any social support variable except coping by using social support ($r=0.41$, $df=50$, $p=0.002$). Using denial was also not correlated with any social support variable. Denial was, however, related to anger, depression, helpless coping, and being black. In a regression model predicting denial, we found that being black ($\beta=0.26$, $t=2.21$, $df=47$, $p=0.03$), being angry ($\beta=0.35$, $t=3.02$, $df=47$, $p=0.004$), and feeling helpless about dealing with AIDS ($\beta=0.38$, $t=3.20$, $df=47$, $p=0.003$) explained 39% of the variance in denial.

DISCUSSION

A major finding of this study was that homosexual HIV-positive men can be characterized as coping with the threat of AIDS by adopting a fighting spirit, reframing stress to maximize personal growth, planning a course of action, and seeking social support. To a large extent, our study subjects scored low on denial and helplessness, and most did not have noteworthy depressive symptoms or current major depression. The low values on denial and helplessness may be due to the subjects' adaptive coping strategies, their asymptomatic status, the nature of subjects who volunteer for an HIV study, and/or the undesirability of admitting to helplessness. The high scores for fighting spirit and the low helplessness scores are consistent with findings from other research studies (8, 13). Interestingly, the HIV-positive subjects scored higher on fighting spirit, helplessness, and denial than did the HIV-negative men. Given that the threat of AIDS is more real and immediate to HIV-positive men, they may more actively mobilize all coping strategies.

We examined the relationship of coping strategies to each other and to measures of dysphoria and self-esteem to determine which coping strategies are associated with more healthy adaptation to HIV infection. Fighting spirit, personal growth, active planning, seeking emotional support, and, to a lesser extent, religious coping appeared to represent similar active or positive coping responses. Denial and helplessness appeared to represent passive and pessimistic coping strategies. As one might expect, helplessness was related to dysphoria and lowered self-esteem, whereas fighting spirit and positive growth tended to be correlated with favorable affect and better self-esteem. These findings support the use of strategies that are emphasized in stress management programs, such as fighting spirit and reframing stress through positive reinterpretation and personal growth. Those who cope with the threat of AIDS by more planning, seeking social support, or turning to religion appear not to be better or worse off with regard to dysphoric mood.

The relative merit or harm of denial (pretending HIV infection has not happened) is less apparent in the available literature. Whereas Greer et al. (6) found that denial had positive survival value in breast cancer

patients, studies in the psychological literature have tended to be less clear about the mental health implications of denial. In our group of HIV-positive homosexual men, it appears that underlying the denial of HIV-positive status were depression, feelings of helplessness, and anger. These findings are consistent with other studies of HIV-infected men (8, 9). Possibly, the HIV-positive individuals who feel overwhelmed by the threat of AIDS express this by more denial, depression, anger, and helplessness.

Finally, we were interested in whether social support is related to particular coping strategies. To a large extent, we found that being satisfied with one's social support networks and participating in the AIDS community were related to more healthy coping strategies (e.g., more fighting spirit, more personal growth, less helplessness). These findings are consistent with previous research (8, 9). Given the cross-sectional design of the present study, however, we cannot determine whether having strong social support leads to enhanced ability to cope with the threat of AIDS or whether those who cope effectively with stress are then better able to elicit social support. These relationships will be studied in our longitudinal follow-up of these subjects. It seems more likely that social support buffers some of the difficulties associated with the threat of AIDS and helps subjects maintain a positive and empowering approach to this disease. Socializing with other HIV-positive men and participating in AIDS support groups, the buddy program, and AIDS organizations may be other ways to help those with HIV infection adapt and perhaps grow from this experience. For homosexual men, who may receive less support from their families, these other sources of support may be critical. Establishing strong social support networks before the onset of HIV-related symptoms may help buffer the mental health consequences of this devastating illness.

The black subjects in our study tended to cope by means of more helplessness, denial, and turning to religion and by less seeking of social support. To some extent, this was due to less satisfaction with their social support networks. It seems that HIV-positive blacks, because they bear the stigma and isolation of race, homosexuality, and HIV infection, should be particularly targeted for social support interventions.

In conclusion, our findings suggest that 1) these subjects primarily coped with the threat of AIDS by adopting a fighting spirit, reframing stress to maximize personal growth, planning a course of action, and seeking social support, 2) more helpless coping, less fighting spirit, and less personal growth were related to dysphoria and poor self-esteem, 3) denial was related to more depression, anger, and helpless coping, 4) satisfaction with one's social support networks and participating in the AIDS community were related to more healthy coping strategies, and 5) black subjects experienced more denial, more helplessness, and less social support. These results suggest that health professionals treating HIV-positive patients should promote a fighting spirit and help patients reframe this health crisis as an opportunity

for personal growth and challenge. Patients who are coping by denial (pretending that HIV infection has not happened) may really be expressing helplessness, anger, or depression and thus may need psychological or psychiatric services. As noted previously (26), patient evaluations should include assessment of available family, friend, and other social support networks. Most important, professionals should encourage patients to use their existing sources of positive social support and should help patients, particularly black patients, find new supports in the community.

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Psychopathology, Hypnotizability, and Dissociation

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Objective: The purpose of the study was to replicate and extend previous findings regarding the hypnotizability of different clinical groups. **Method:** The authors compared the differential hypnotizability of four psychiatric groups—patients with dissociative disorders (N=17), schizophrenia (N=13), mood disorders (N=13), and anxiety disorders (N=14)—and one normal group of college students (N=63). Hypnotizability was assessed by four different measures: the eye roll sign and the induction score of the Hypnotic Induction Profile, the Stanford Hypnotic Susceptibility Scale, Form C, and two self-ratings of hypnotizability. **Results:** As predicted, dissociative disorder patients had significantly higher hypnotizability scores on all measures than all other groups. Schizophrenic patients, on the other hand, had significantly lower scores than normal subjects on the eye roll sign and induction score but not on the other measures of hypnotizability. Some other unpredicted between-group differences were also found. Nevertheless, despite the between-group differences, the intercorrelations between the various hypnotizability measures within the normal group were very similar to those observed in the combined patient groups. **Conclusions:** The findings suggest that routine hypnotizability assessment may be useful in the differential diagnosis of patients with dissociative disorders. (Am J Psychiatry 1992; 149:1521–1525)

The relationship between psychopathology, hypnotizability, and dissociation has received increasing attention over the last decade (1–11). The major methodological focus of these reports has been on developing a better understanding of different kinds of psychopathology by studying the hypnotizability scores of different clinical groups. For example, because of the historical association between hypnotizability and dissociation, patients suffering from dissociative disorders or other psychiatric syndromes that have a hypothesized dissociative component were predicted to have significantly higher hypnotizability scores than normal subjects or patients with nondissociative conditions (1, 2, 4, 11, 12). In contrast, others predicted that patients with certain kinds of psychiatric illnesses, such as schizophrenia, should have significantly lower hypnotizability scores than normal subjects or other clinical groups (9, 11, 13). A growing number of studies have tested each of these predictions (4, 9, 14). Unfortunately, no clear pattern of findings has emerged, and

empirical support for each of these predictions appears to be moderated by both the type of clinical disorder studied and the type of hypnotizability scale employed (4, 9, 14). Therefore, before further studies are carried out, it would be wise to consider what types of clinical patients are expected to be more or less hypnotizable than normal subjects and what types of hypnotizability scales are most likely to detect significant differences between these groups.

There are many different methods for measuring individual differences in responsivity to hypnosis, such as the Barber Suggestibility Scale (15), the Stanford Hypnotic Susceptibility Scales (16–18), the Hypnotic Induction Profile (11, 19), and various self-rating procedures (20). While scores on these tests correlate positively (21, 22), the intercorrelations are not high enough ($r=0.6$ – 0.7) to consider these different instruments as interchangeable measures. Hence, some clinical groups may score significantly higher or lower than normal subjects on one type of hypnotizability measure but not on another.

What type of clinical groups are expected to be significantly more or less hypnotizable than “normal” subjects? (Note that most studies have assumed that college students are an appropriate normal comparison group.) Historically, patients suffering from dissociative disorders (e.g., multiple personality disorder or psychogenic fugue) have been considered by most to be significantly more hypnotizable than normal subjects

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(23, 24). This prediction has received some empirical confirmation. For example, Bliss (1) has reported that two different samples of patients suffering from multiple personality disorder had significantly higher mean scores on the Stanford Hypnotic Susceptibility Scale, Form C (18), than normal subjects. Unfortunately, no data were reported on the reliability of the diagnosis of multiple personality disorder and no other types of dissociative disorder patients were studied.

Two other types of clinical groups that have been hypothesized to have a dissociative component to their psychiatric symptoms—patients suffering from post-traumatic stress disorder (PTSD) (25–27) and phobic patients (2)—have also been studied. Hence, these kinds of patients were also expected to have significantly higher mean hypnotizability scores than normal subjects. For patients with PTSD, this prediction has been confirmed in two separate studies. For example, Stutman and Bliss (27) found that patients with PTSD had a significantly higher mean score on the Stanford Form C than normal subjects. Spiegel and associates (26) reported a similar finding with the Hypnotic Induction Profile. However, no clear pattern of findings has emerged regarding the higher hypnotizability of phobic patients. For example, several studies have found that phobic patients were more hypnotizable than normal subjects (2, 28–31), others found no significant between-group differences (32, 33), and another study observed that phobic patients were significantly less hypnotizable than normal subjects (34).

Finally, other clinical disorders that have been hypothesized to have a dissociative component are conversion disorders, histrionic personality disorders, and mixed personality disorders. However, only one study has found that patients with these kinds of diagnoses have significantly higher mean hypnotizability scores than normal subjects (E.J. Frischholz et al., unpublished 1991 paper).

On the other hand, it has been hypothesized that schizophrenic patients are significantly less hypnotizable than normal subjects because of some type of attention or concentration deficit (11). However, this finding appears to obtain only for scores on the Hypnotic Induction Profile (8, 9, 11; unpublished 1991 paper of E.J. Frischholz et al.), not for the Stanford Form C (4). The study by Pettinati et al. (8) is particularly interesting in this regard, since both the Hypnotic Induction Profile and the Stanford Form C were employed. In that study, schizophrenic patients had significantly lower Hypnotic Induction Profile scores than normal subjects but mean scores similar to those of normal subjects on the Stanford Form C. This finding was obtained despite a correlation of 0.55 between scores on the Hypnotic Induction Profile and Stanford Form C. Finally, one recent study (7) reported that the mean Hypnotic Induction Profile score for six schizophrenic patients was not significantly different from the reported mean score for normal subjects.

Collectively, these findings suggest that further research is necessary to document what types of psychi-

atric syndromes are characterized by hypnotizability that is higher or lower than normal. Such research should study groups that are expected to have hypnotizability scores that are higher or lower than those of normal subjects, and multiple measures of hypnotic responsiveness should be employed. Furthermore, the clinical groups should be independently and reliably diagnosed according to standardized criteria, and the interrater reliability of the various hypnotizability scores should be demonstrated.

METHOD

The purpose of the present study was to replicate and extend previous findings regarding the hypnotizability of different clinical groups. Five groups were studied: dissociative disorder patients, schizophrenic patients, anxiety disorder patients, mood disorder patients, and college students (i.e., "normal" subjects). All subjects were volunteers in experiments that required the routine administration of the Hypnotic Induction Profile, Stanford Form C, and two self-ratings of hypnotizability taken immediately after the objective scales were given. All patients in the four clinical groups were independently diagnosed according to *DSM-III* and *DSM-III-R* criteria by both a psychiatrist and a clinical psychologist. Patients were included in the present study only if both mental health professionals agreed on their diagnosis. Hypnotizability examiners were unaware of the patients' diagnosis at the time of testing.

Seventeen patients with a primary diagnosis of dissociative disorder were tested. Seventy-one percent ($N=12$) had a diagnosis of multiple personality disorder, while the other 29% ($N=5$) had a diagnosis of dissociative disorder not otherwise specified. All of these patients were women, and their mean age was 35.1 years ($SD=9.7$). Ten patients were taking psychiatric medication.

All 13 schizophrenic patients were diagnosed as schizophrenic, paranoid type. Seventy-seven percent ($N=10$) were men, and the mean age was 37.6 years ($SD=8.0$). All of the patients were taking antipsychotic medication.

Of the 14 subjects in the anxiety disorder group, 7% ($N=1$) had a diagnosis of generalized anxiety disorder, 14% ($N=2$) had a diagnosis of simple phobia, 14% had a diagnosis of agoraphobia without panic disorder, 29% ($N=4$) had a diagnosis of panic disorder with agoraphobia, and 36% ($N=5$) had a diagnosis of panic disorder without agoraphobia. Fifty percent of the subjects were men, and the mean age was 33.9 years ($SD=8.1$). Nine patients were taking antianxiety medication.

Of the 13 subjects in the mood disorder group, 31% ($N=4$) were suffering from major depression (single episode), 39% ($N=5$) had recurrent major depression, 23% ($N=3$) had bipolar disorder, and 7% ($N=1$) had a dysthymic disorder. Ninety-two percent ($N=12$) of the group were women, and the mean age was 45.6 years ($SD=10.4$). Eight patients were taking antidepressant medication.

TABLE 1. Hypnotizability Scores for Psychiatric Patients in Four Diagnostic Groups and in Normal Subjects

		Hypnotic Induction Profile						Stanford Hypnotic Susceptibility Scale, Form C			
		Eye Roll Sign Score		Induction				Objective Score		Self-Rating	
				Score		Self-Rating					
Group	N	Mean ^a	SD	Mean ^a	SD	Mean ^a	SD	Mean ^a	SD	Mean ^a	SD
Psychiatric patients diagnosed with <i>DSM-III</i> and <i>DSM-III-R</i>											
Dissociative disorder	17	3.38 _a	0.67	8.05 _a	2.42	6.42 _a	2.03	8.94 _a	1.43	7.47 _a	2.07
Schizophrenic disorder	13	1.73 _b	0.90	3.73 _b	2.13	4.31 _c	1.93	5.69 _c	1.38	5.15 _c	2.44
Mood disorder	13	1.88 _b	0.93	5.13 _{b,c}	3.07	4.98 _{a,c}	3.37	5.85 _c	2.51	6.12 _{a,c}	3.02
Anxiety disorder	14	3.02 _a	0.74	6.48 _c	2.62	4.82 _{a,c}	2.64	6.64 _c	2.13	6.86 _{a,c}	2.06
College students	63	2.52 _c	0.68	6.59 _c	2.98	4.14 _c	2.33	6.16 _c	3.46	5.92 _c	2.76

^aMeans that do not share the same column subscript are significantly different from one another at the 0.05 level (Duncan's multiple range test).

Sixty-three college undergraduates served as the normal comparison group. Sixty percent (N=38) were male, and the mean age was 20.9 years (SD=3.7).

RESULTS

Interrater Reliability of Hypnotizability Scores

Different examiners readministered the Hypnotic Induction Profile and Stanford Form C to 31 subjects from the four clinical groups within a week's time. Relative interrater reliability coefficients were computed using an intraclass correlation model discussed by Shrout and Fleiss (35). The interrater reliability was 0.95 for the eye roll sign score of the Hypnotic Induction Profile, 0.90 for the induction score of the Hypnotic Induction Profile, and 0.95 for Stanford Form C scores. Collectively, these findings indicate that hypnotizability scores on each of the two different scales were highly reliable over both examiners and a week's time.

Hypnotizability Scores Among Clinical and Normal Groups

The means and standard deviations for each hypnotizability measure cross-classified by normal/clinical group are presented in table 1. A two-way multivariate analysis of variance (MANOVA) was first computed with hypnotizability scores as the dependent variables and medication status (medication versus no medication) and clinical diagnosis (dissociative disorder, anxiety disorder, and mood disorder) as the independent variables. The results indicated a significant main effect for clinical diagnosis ($p < 0.01$). However, no significant effects for medication status or the medication status/clinical diagnosis interaction were observed. Therefore, a one-way MANOVA was used to compare the differences between mean scores for the various clinical/normal groups. This analysis indicated that significant differences between groups were present ($F = 4.37$, $df = 20$, 438 , $p < 0.001$). Individual analyses of variance and special contrasts were then calculated to further clarify the nature of these differences.

It is clear from the findings presented in table 1 that dissociative disorder patients had significantly higher mean scores on every measure of hypnotizability than all other clinical and normal groups. In contrast, schizophrenic patients had significantly lower mean eye roll scores and induction scores than normal subjects and anxiety disorder patients, but they did not have significantly lower scores on the Stanford Form C or either of the self-ratings of hypnotizability. Finally, although mood disorder patients had significantly lower mean eye roll scores than normal subjects, they did not have significantly lower mean induction scores than normal subjects, as has been found in previous studies (8, 9, 11; unpublished paper of E.J. Frischholz et al.).

Correlations Between Hypnotizability Measures

The correlations between the various hypnotizability measures within the normal group (N=63) and combined clinical groups (N=57) are presented in table 2. All of the hypnotizability measures intercorrelated positively (range of r values=0.25–0.78) and were significant at the 0.05 level (two-tailed). In addition, the correlations between measures were not significantly different from one another in comparisons of the matrices for the normal group (average $r = 0.54$) and combined clinical groups (average $r = 0.53$). However, it is clear that the eye roll score correlated lower with the other measures of hypnotizability. Hence, one can conclude that the eye roll probably does measure the same thing as the other measures of hypnotizability.

DISCUSSION

The findings of the present study suggest that routine hypnotizability assessment may be useful in the differential diagnosis of patients with dissociative disorders from normal subjects and patients with other types of psychopathology. In spite of the variability in the specificity and sensitivity of the hypnosis measures, dissociative disorder patients were observed to have significantly higher hypnotizability scores on various measures than all other groups had. This is consistent

TABLE 2. Correlations Between Measures of Hypnotizability in Normal Subjects (N=63) and in Psychiatric Patients (N=57)

Measure and Group	Correlation (r) ^a			Stanford Hypnotic Susceptibility Scale, Form C, Objective Score
	Eye Roll Sign Score	Induction Score	Induction Self-Rating	
Induction Score				
Normal	0.25			
Clinical	0.52			
Induction self-rating				
Normal	0.27	0.65		
Clinical	0.29	0.59		
Stanford Hypnotic Susceptibility Scale score, Form C				
Normal	0.44	0.63	0.55	
Clinical	0.60	0.72	0.56	
Stanford Hypnotic Susceptibility Scale, Form C, self-rating				
Normal	0.43	0.67	0.78	0.70
Clinical	0.31	0.55	0.65	0.47

^aAll correlations are significant at the 0.05 level (two-tailed).

with the previous findings reported by Bliss (1) and the classic clinical observations of Janet (23), Prince (24), and contemporary investigators (5, 11). In addition, contrary to the opinion expressed by Frankel (12), the findings support a theoretical and empirical relationship between the constructs of dissociation and hypnotizability.

The findings also provide support for the contention (11) that schizophrenic patients have significantly lower eye roll sign and induction scores than normal subjects but not lower scores on the two self-ratings of hypnotizability (self-rating induction measure and self-rating Stanford Form C) or the Stanford Form C scale. Again, these results replicate the findings of most other studies (4, 8, 9, 11; unpublished 1991 paper of E.J. Frischholz et al.; *DSM-III-R*) but not the methodologically flawed, small sample study reported by Murray-Jobsis (7). Interestingly, this finding was observed despite significant intercorrelations between eye roll sign and induction scores and the other measures of hypnotizability. For example, induction scores correlated ($r=0.72$) with Stanford Form C scores in the combined clinical groups. Yet induction scores were sensitive to differences between schizophrenic patients and normal subjects, while Stanford Form C scores were not. Further research is necessary to determine why eye roll sign and induction scores, despite their significant intercorrelations with other measures of hypnotizability, significantly discriminate between normal subjects and schizophrenic patients.

Surprisingly, mood disorder patients did not have significantly lower induction scores than normal subjects did, as they have been found to do in other studies (4, 8; unpublished paper of E.J. Frischholz et al.). However, the induction score for mood disorder patients in the present study (mean=5.13) was not significantly different from that observed in the study by Pettinati et al. (8) (mean=5.49). This suggests that the failure to find a significant difference between mood disorder patients

and normal subjects in the present study may be due to a smaller sample size, since the differences are in the predicted direction. Consistent with the findings of other studies, mood disorder patients did not have significantly different mean Stanford Form C scores than normal subjects had (8).

Similarly, anxiety disorder patients in the present study did not have significantly different hypnotizability scores than normal subjects. However, this may be because only 14% of the patients in this group had a phobic diagnosis. Phobic patients have been found to have significantly higher hypnotizability scores than normal subjects in some studies (2, 28–31) but not in others (32–34). In addition, none of the anxiety disorder patients in the present study was suffering from PTSD. Patients with PTSD have been observed to have significantly higher mean hypnotizability scores than normal subjects in other studies (26, 27). Further research is necessary to determine what type of anxiety disorder patients have significantly higher or lower hypnotizability scores than normal subjects.

As has been found in previous investigations (36–38), medication status did not appear to moderate differences in hypnotizability between the clinical groups in the present study when it was possible to test this hypothesis. It was not possible to test the hypothesis in the schizophrenic group because all of the patients were taking antipsychotic medication. However, medication status has not been found to significantly affect the hypnotizability scores of schizophrenic patients in other studies (36–38).

Collectively, the results of the present study highlight the clinical and theoretical utility of studying hypnotizability differences between various normal and abnormal groups and between the choice of hypnotizability measures. Undoubtedly, some groups are consistently more or less hypnotizable than others, although these relationships appear to be moderated by the type of normal or abnormal group studied and the type of hyp-

notizability scale employed. Furthermore, issues of reliability of diagnosis and hypnotizability score must also be addressed before any firm conclusions can be drawn. Nevertheless, the findings of the present study and previous investigations clearly indicate that dissociative disorder patients are more hypnotizable than normal subjects or other clinical groups.

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A Historical Perspective on the Role of State Hospitals Viewed From the Era of the "Revolving Door"

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***Objective:** By focusing on the functioning of a state hospital throughout its existence, the author provides a historical perspective on the nature and causes of "revolving door" admissions. **Method:** Northampton State Hospital was chosen as a prototype, and data on characteristics of patients and patterns of hospital utilization were analyzed from three 10-year periods: 1880–1889, 1930–1939, and 1980–1989. The data for the first two time periods came from the hospital's admission and discharge logbooks and its annual reports; the material for the most recent decade was obtained from unpublished yearly reports generated by the hospital's medical records department. **Results:** The hospital operated very differently in each of the decades analyzed, but only in the 1980s was recidivism a major finding. This was not, as has often been thought, due to problems or populations unique to the state hospital in the 1980s nor to the fact that in earlier eras the state hospital rarely discharged patients. The once-large asylum has been replaced by a facility rapidly admitting and discharging patients, many of whom have accumulated more than 10 lifetime admissions, in a pattern of care not previously noted. **Conclusions:** State hospitals have functioned in different yet questionable ways throughout their history. Their current role of providing a revolving-door pattern of care to a considerable population is rooted in a contemporary shift in ideology. This role for state hospitals appears to make no more sense than did their earlier role as neglected and neglectful asylums, and it should be reevaluated.*

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The literature has given them a multitude of labels—"recidivists," "revolving-door patients," "patients who return," "patients with frequent rehospitalizations," "heavy users," "patients with repeat admissions," "patients with recurrent psychiatric hospitalizations"; service providers experience them as legion; and the resources required for meeting their needs can be enormous. These are the persons with serious and persistent mental illness who have gone back and forth between public sector inpatient settings and the community in a pattern of care (or lack of care) often referred to as an unfortunate and unexpected consequence of deinstitutionalization.

Recidivism in contemporary public sector psychiatric settings can be viewed as a byproduct of clashes between two competing ideologies and their resultant clinical practices. The two ideologies are paternalism and autonomy. The competing loci of care and treat-

ment are the state hospital and the community. The battlefields are the allocation of resources to each and the statutes that determine who goes where. The casualties of this clash are the patients. And the unfortunate foot soldiers are the staffs, be they in state hospitals, community mental health centers, or any community program.

While recidivism appears to be uniquely contemporary, the tensions I have mentioned are not at all peculiar to our era. The issues thought to contribute heavily to the phenomenon of recidivism can be found clearly described in nineteenth-century publications. For example, on the issue of paternalistic commitment versus autonomy in the community, note the following from an 1883 issue of the *Alienist and Neurologist*: "We owe the harmless lunatic a duty to save him from perpetual lunacy if we can. To leave him wholly to himself, even though he hurts no one, is not always kind. Such a course endangers incurable chronicity, and this is cruel to him" (1).

On the threshold for determining dangerousness, note this from the same publication in 1883: "[If] unreasonable and unjust obstacles were not every day thrown in the way of committing the insane to the asylums whose care and treatment is their due, and whose

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restraint is their right and the community's protection, murder by sane lunatics would be less frequent. Suppress the liberation epidemics" (2).

On the conditions of state hospitals, note these remarks from an 1885 issue of the *American Journal of Insanity*: "[Danvers State Hospital] has been a disgrace to the Commonwealth . . . One to two hundred patients have been obliged to occupy beds placed upon the floors . . . , personal privacy has been interfered with, . . . attendants and physicians have been wearied . . . [It is] 'a convenient dumping ground for all cases of degenerative nervous diseases attended with mental failure' which are disagreeable to care for elsewhere or whose care elsewhere costs more than at the asylum" (3).

Public sector inpatient recidivism is not simply a fall-out from current difficulties in providing care and treatment to persons with serious and persistent mental illness, because many of these difficulties existed before there appears to have been widespread recidivism. The revolving door is a phenomenon of the current ideologies that are the underpinnings of deinstitutionalization and the resultant role assigned to the state hospital.

Recent overviews of the policy of deinstitutionalization have dissected in great detail the ideologies and economics of deinstitutionalization, but they have not paid sufficient attention to the historical and contemporary role of the state hospital (4-6). One manner in which to understand the past roles and current functioning of state hospitals, and how these fit into the deinstitutionalization phenomenon, is to examine recidivism. Such an examination should help focus the debate about the future role of the state hospital.

To this end, I have used one state hospital, Northampton State Hospital, as the prototype and present data from three decades within 100 years. I chose this hospital because it has been in the vanguard of "second-generation deinstitutionalization" (7, 8) and the focus of considerable study. The data for this analysis came from the annual reports and admission/discharge log-books of Northampton State Hospital for the decades 1880-1889 (9, 10) and 1930-1939 (11-13) and from unpublished annual reports generated by the medical records department of the hospital for 1980-1989. The information on the nineteenth-century recidivists discussed in this article comes from patient and court records.

1880-1889

In the 1880 census of the United States, there was one insane person to every 545 inhabitants, or 91,997 insane persons. In 1886 there were 121 asylums (public and private), with at least one state institution in each of the 38 states except Vermont and Delaware, and 61,411 patients were treated in those asylums by medical staffs that totaled 377 physicians. Most of the states were struggling under the financial constraints of caring for the insane, particularly because of the increasing demands of chronic cases (14). There was excitement

about the "unparalleled progress" in psychiatry that allowed for a "scientific and positive basis for treatment in many cases of insanity which before was unattainable" (14). New medications abounded, violence on wards with refractory patients was diminishing, use of seclusion and restraint was decreasing, unlocked wards were common, occupational therapy was highly valued, and individual treatment plans were a "keynote of progress" (14).

It is within this climate that the functioning of Northampton State Hospital yielded the data presented in the first columns of tables 1 and 2. A closer look at 1 year is worthwhile. In 1886, the first year following the retirement of its illustrious superintendent, Pliny Earle, Northampton State Hospital had a year-end census of 491 patients. Edward Nims, the new superintendent, noted that 1886 was unusual in that the number of admissions was greater than it had been in previous years, including 25 patients transferred from Danvers Lunatic Hospital because of overcrowding there. Nims also noted a decrease in census due to the removal of 33 chronic patients to almshouses and 12 patients to family care, to be supported there, at the same cost as if they had been in the hospital, by the Board of Lunacy and Charity. Patients in the hospital worked at the farm, kitchen, sewing room, laundry, mattress room, ornamental grounds, stable, bakery, boiler room, carpenter shop, and wards. Indeed, the patients' labor was integral to the functioning of the hospital, as there were but 74 persons employed there; the personnel budget was \$28,969.39.

In 1886 there were 176 persons (80 male and 96 female) admitted for a total of 183 admissions; during the year seven persons were admitted twice. Of the 135 persons admitted for the first time, eight were less than 20 years of age and eight were over 60 years old. Of all persons admitted, the most common causes of insanity were (in decreasing order of frequency) intemperance, ill health, overwork, epilepsy, and masturbation. The admission diagnoses were mania (N=117), dementia (N=27), melancholia (N=22), epilepsy (N=11), general paralysis of the insane (N=4), inebriate (N=1), and no insanity (N=1).

In 1886 there were 168 discharges, which included 26 patients who died. Of the other discharges, 29 patients were recovered, 10 much improved, 59 improved, 43 unimproved, and one not insane. Of the 29 patients who recovered, 23 were hospitalized less than 1 year; of these, 13 were hospitalized less than 3 months. The 26 deaths included 16 patients who died of chronic diseases, eight who died of acute disorders (two of them of exhaustion from mania), and two who died of old age. Fourteen who died had been hospitalized less than 1 year, and 17 were more than 50 years old.

Finally, it is worth noting that the 1886 total expenditures for Northampton State Hospital were \$94,851.91, approximately \$3,000 less than the total receipts.

During the decade 1880-1889, Northampton State Hospital had a stable mean census of 466 (SD=14). The

TABLE 1. Characteristics of Northampton State Hospital Patients in 1880-1889, 1930-1939, and 1980-1989

Item	1880-1889		1930-1939		1980-1989	
	Diagnosis	Percent of Patients	Diagnosis	Percent of Patients	Diagnosis	Percent of Patients
Gender in average daily census						
Male ^a		49.6		45.8		58.0
Female ^b		50.4		54.2		42.0
Age at first admission (years)						
<20		5.3		3.9		10.5
20-29		27.0		14.7		39.9
30-39		25.7		17.9		25.1
40-49		19.6		18.1		12.2
50-59		11.0		15.0		6.3
60-69		7.1		13.5		3.8
≥70		4.2		16.9		2.0
Rank order of diagnoses at first admission						
1	Mania	65.0	Dementia praecox	24.4	Schizophrenia	18.2
2	Melancholia	17.4	Psychosis with cerebral arteriosclerosis	14.4	Depressive disorders	12.5
3	Dementia	16.9	Senile psychosis	10.4	Bipolar disorder	6.6
4	Epilepsy	5.1	Alcoholic psychosis	8.4	Substance-related disorders	6.6
5	General paralysis	2.7	Manic-depressive psychosis	8.3	Other psychosis	5.9
6	Inebriate	1.8	Syphilitic meningo-encephalitis	5.3	Alcohol-related disorders	5.7
7			Involuntary psychosis	5.0	Personality disorders	3.8
8			Psychosis with mental deficiency	4.4	Schizoaffective disorder	3.4

^aFor 1880-1889, mean number=231; for 1930-1939, mean number=959; for 1980-1989, mean number=123.

^bFor 1880-1889, mean number=235; for 1930-1939, mean number=1,135; for 1980-1989, mean number=89.

hospital's admissions numbered about one-third of its census, so that the turnover rate for a bed was every 3 years. First admissions accounted for three-quarters of all admissions, and most admissions were of persons between 20 and 60 years of age. Few persons accumulated high numbers of lifetime admissions. Only eight persons had had more than five lifetime admissions by 1889; two of these individuals had had more than 10 admissions. While patients who were discharged as recovered had comparatively short stays, 81% of the patients at the year-end census had stays in excess of 1 year. Twenty-one percent of the discharges were accounted for by deaths. This group was a mixture of long-stay patients and those with shorter stays; a majority were over 50 years old. While the hospital fulfilled many functions during the decade—it was both an acute care facility and a long-term care facility—it was not a repository for geriatric patients, it did not keep patients whose improvement allowed their discharge, and it did not have a revolving-door population.

1930-1936

In 1936 there were 523 psychiatric hospitals in the United States, which provided care to 566,482 patients. Of these hospitals, 172 were state hospitals ranging in size from less than 1,500 patients (N=45) to over 6,000

patients (N=3). Medical staff coverage ranged from one physician for 125 patients to one for 1001 (15, 16). State hospitals were thought to be greatly improved (16, 17), but overcrowding (18) and political interference (19, 20) were major problems. Training and research were encouraged at state hospitals (21, 22), as was the use of the *New Standard Nomenclature of Diseases* (23).

Treatments in use in hospitals included rest (24), continuous baths (24) and wet packs (25), insulin coma and metrazol-induced convulsive therapy (26, 27), irradiation (28), sodium Amytal (29), and psychotherapy (16, 30). There were calls for community care (31) and for general hospital psychiatry wards (24).

In 1930 Massachusetts was expending approximately 20% of its annual budget for the care of mental patients (32). Northampton State Hospital was one of 13 state hospitals devoted to the care of persons with mental disease (33). The data for Northampton State Hospital from 1930 to 1939 are presented in the second columns of tables 1 and 2. An analysis of 1 year in detail shows that in 1936, Northampton State Hospital was undergoing expansion through construction projects under the WPA but nonetheless was experiencing overcrowding. High local unemployment allowed for a good caliber of persons to be employed as attendants. New treatments included malaria treatments for patients with neurosyphilis and sodium Amytal for catatonic patients.

The year-end census of 2,229 patients (1,028 male

TABLE 2. Northampton State Hospital Utilization Patterns in 1880-1889, 1930-1939, and 1980-1989

Item	1880-1889	1930-1939	1980-1989
Census			
Mean daily census	466	—	212
Mean year-end census	466	2,094	212
Range of census	451-479	1,699-2,387	297-138 ^a
Percent change in census	6	40	-54
Admissions/discharges			
Mean number of admissions	144	575	935
Mean number of first admissions	108	453	282
First admissions as percent of total admissions	75	79	30
Mean number of discharges	143	508	958
Ratio of admissions to discharges	1.01:1	1.13:1	0.98:1
Ratio of admissions to census	0.31:1	0.27:1	4.41:1
Mean number of deaths	30	162	3
Deaths as a percent of discharges	21	32	0.3
Length of stay of discharged patients (days)			
Mean for decade	1,097	197	92
Lowest mean	791 (1880)	175 (1939)	47 (1988)
Highest mean	1,386 (1886)	214 (1931)	288 (1980)
Year-end census of patients with lengths of stay <1 year			
Mean percent for decade	19		63
Lowest percent	14 (1880)		53 (1980)
Highest percent	26 (1888)		77 (1986)
Length of stay of first-admission patients at year-end census (years)			
Lowest mean		4.55 (1934)	0.24 (1988)
Highest mean		8.42 (1939)	14.40 (1980)
Length of stay of discharged patients (cumulative %)			
≤30 days	8.5	20.0	64.3
≤90 days	29.3	38.1	83.0
≤180 days	37.2	51.6	89.9
≤1 year	59.2	63.7	94.8
Recidivism			
Rate (repeat admissions as percent of total admissions)	24	21	70
Year-end census of patients with ≥10 admissions			
Mean number	<1	<1	30
Lowest percent	0	0	4.2 (1981)
Highest percent	0.2	0.04	22.7 (1989)

^aNumbers declined over the decade.

and 1,201 female) included 1,871 patients in the hospital and 358 on visit. The major diagnostic categories of the patients in the hospital were dementia praecox (20%), psychosis with cerebral arteriosclerosis (8%), mental deficiency (7%), manic depression (6.5%), psychosis secondary to alcohol (6%), involutional psychosis (5%), CNS syphilis (4.5%), and senile psychosis (4.5%). Four hundred thirty-three of the year-end census patients represented readmissions; 268 (62%) of these were diagnosed as having dementia praecox.

In 1936 there were 619 admissions, eight of which were voluntary. The diagnostic distribution of these admissions was similar to that of the year-end census except that the diagnoses of psychosis with cerebral arteriosclerosis and psychopathic personality were a much higher percentage of the admissions than of the year-end census. Five hundred ten (82%) of the admissions were first admissions. The age distribution was significant in that 33% of the patients with first admissions were over 60 years of age. Nineteen percent of them were over 70 years old, and 98% of these had either psychosis secondary to cerebral arteriosclerosis or senile psychosis. Of all the patients who returned from visit status in 1936, only 58 had been out of the hospital for more than 1 month.

There were 568 discharges—351 to the community, 64 to other mental hospitals, and 153 representing patients who died. Of the discharges to the community, 65 (19%) of the patients had recovered, 211 (60%) were improved, 32 (9%) were unimproved, and 43 (12%) were without psychosis. Of the 147 patients who died in the hospital, 75 (51%) were more than 70 years of age. Of these, 82% had a primary psychiatric diagnosis of either psychosis secondary to cerebral arteriosclerosis or senile psychosis. Of the 83 patients who died with one of these two diagnoses, 38 (46%) had been hospitalized less than 4 months and 56 (67%) had been hospitalized less than 1 year.

In summary, during the decade 1930-1939, Northampton State Hospital had a census that increased by 40%, and the census was more than 2,000 patients from 1933 on. The mean number of admissions for the decade—575 (SD=58)—represented one-quarter of the census; hence the turnover rate for a bed was once every 4 years. Seventy-nine percent of all admissions were first admissions. Of these, 30% were of persons over the age of 60 and 15%-20% were of persons over 70 years of age. Almost all the patients admitted who were over 70 years old had psychosis secondary to either cerebral arteriosclerosis or senility. Of the mean of 508

(SD=85) discharges each year, an average of 32% were due to death. Many of those who died were older patients, most of whom had been hospitalized a comparatively short time. The patients who remained in the hospital did so for progressively longer times, so that by 1939 the mean length of stay of all first-admission patients in the hospital at year end was 8.42 years and of all readmitted patients was 8.76 years. Northampton State Hospital continued to admit and treat persons with serious and persistent mental illness—more than one-half of its year-end census who were readmitted patients had dementia praecox. But the facility had become one to which elderly, debilitated, senile individuals were sent, often to die within a year of their admission. There is no indication that many patients had frequent admissions and discharges; only three patients admitted during this decade had 10 or more lifetime admissions.

1980–1989

In 1984 a point-in-time census of all state and county mental hospitals in the United States indicated that there were 118,647 patients, which was 79% below the peak census of 558,922 patients recorded in 1955. Some states had decreased their public mental hospitals' census by more than 90% (4).

In 1986 there were 3,039 facilities providing inpatient services, of which 285 were state and county mental hospitals. These public hospitals accounted for 21.6% of the 2,055,571 total inpatient care episodes. Three-quarters of all patient care episodes at state and county mental hospitals were inpatient care episodes (34). By 1990 services for persons with serious mental illness were described as a "disaster," and deinstitutionalization was labeled a "hoax" (5). More persons with serious and persistent mental illness were in jails, prisons, or public shelters and on the streets than were in public mental hospitals (4).

During the 1980s Massachusetts' expenditure for mental health and retardation services increased by \$543 million, or 150%, from 1980 through 1988 (Massachusetts State Senate Committee on Ways and Means, Fiscal Year 1990 Budget Recommendations, June 1989). During this decade Northampton State Hospital, being the beneficiary of a federal court consent decree mandating treatment in the least restrictive suitable alternative (7), entered the forefront of deinstitutionalization. During the first 10 years the decree was in effect (1978–1988), Northampton State Hospital discharged *every* patient who had been in the hospital on the day the decree was signed (8). Data describing Northampton State Hospital in the 1980s are shown in the third columns of tables 1 and 2. From 1980 to 1989 the Northampton State Hospital census fell by 54%, and admissions decreased by 36%. Throughout the decade only 30% of all admissions were first admissions. The turnover rate of a bed at the hospital was approximately 5 times per year. Virtually all discharges were to commu-

nity settings, and the number of deaths (including deaths in general hospitals shortly after discharge) never constituted more than 0.5% of the number of discharges. Almost 95% of all discharges were after stays of less than 1 year, and the mean length of stay of discharged patients decreased by 84% throughout the decade.

The length of stay of patients in the hospital at the year-end census decreased dramatically. The mean length of stay of all first-admission patients decreased by 98%, from 14.4 years to 87 days. In 1988 no first-admission patient in the hospital had been there as long as 1 year. While patients in the hospital had shorter stays, a progressively greater percentage of them had had prior admissions, and the number of patients with 10 or more prior admissions increased annually.

A more detailed analysis of 1 year's data shows that in 1986, the year-end census of Northampton State Hospital was 226 patients (142 male and 84 female). Of these, 209 (92%) were in the hospital, 15 (7%) were on visit, and two (1%) had escaped. The length of stay in this year-end census ranged from 1 day to 23.5 years, with 9% of the population on the census less than 1 week, 29% less than 1 month, 45% less than 3 months, and 79% less than one year. In the year-end census there were 12 patients (5%) over the age of 65 years; half of these had stays of less than 6 months. A point-in-time study showed the diagnostic mix of patients in the census to be schizophrenia, 54%; affective disorder, 17%; organic brain syndrome, 8%; mental retardation, 4%; and all other diagnoses, 18%.

In 1986 there were 864 admissions (523 male and 341 female patients). Of these, 74 (9%) were less than 21 years of age, and 30 (4%) were more than 65 years old. The 864 admissions were accounted for by 655 different patients. One hundred forty patients had more than one admission in 1986. The mean length of stay of this group was 37 days, with a mean length of time between admissions of 70 days. The highest number of admissions that occurred in 1986 for any one patient was 13; this patient had accumulated 83 lifetime admissions over the 10-year period ending in 1986.

There were 823 discharges in 1986. Of these, 60% occurred after stays of less than 1 month, 81% after less than 3 months, and 93% after less than 1 year. Three patients died, all of whom were 75 years old or older; their lengths of stay were 4 years, 7.5 years, and 57 years.

COMPARISON OF THE THREE DECADES

From tables 1 and 2, a comparison of the operation of Northampton State Hospital in the 1880s, the 1930s, and the 1980s can be made. This compilation shows that the state hospital functioned very differently at each of these periods. During the 1980s, unlike before, it was a shrinking facility, with ever shorter lengths of stay. It no longer admitted many elderly infirm patients, as it had in the 1930s, and it had discharged much of the preexisting geriatric population; hence there were very few deaths. This difference in the death rate means

that a much higher percentage of patients discharged each year were potential readmissions, since deceased patients can obviously not be readmitted. But the difference in the death rate does not in and of itself account for the difference in the recidivism rate. If the facility had been operating in the 1980s as it had earlier, there would not have been as dramatic a difference in the ratio of admissions to census as there was. If anything, the higher death rates in the two earlier time periods would lessen this difference. More and more of the admissions were accounted for by patients with prior admissions. Further, individual patients accrued successively more admissions, in a pattern of care not previously noted in the 1880s or the 1930s.

During the 1980s the proportion of patients in the hospital at the year-end census who had 10 or more lifetime admissions ranged from 4.2% to 22.7% and averaged 14%. The number of patients with 10 or more admissions during the first 50 years of operation of Northampton State Hospital (1858–1908) numbered two. They were brother and sister. It is instructive in this historical review to provide a brief account of the two patients whose pattern of use foreshadowed modern trends of recidivism.

TWO NINETEENTH-CENTURY RECIDIVISTS

Case 1. Ms. A was a 40-year-old single woman living in the family home at the time of her first admission to Northampton State Hospital in 1867. She had had attacks of insanity of short duration for 12 years before her first admission. A younger sister had been briefly hospitalized at Northampton State Hospital 2 years earlier. Ms. A's family history revealed that the mother and several of the mother's siblings had been deemed insane.

Between 1867 and 1886 Ms. A was involuntarily admitted to Northampton State Hospital 17 times. Her mean length of stay for the first 15 admissions was 80 days (range=26–169 days), and her community tenure between admissions ranged from 13 days to 934 days.

Over the course of her first 16 admissions, Ms. A was discharged as recovered 12 times, much improved once, improved twice, and with no result noted once. Her illness was characterized by "sudden relapses of irregular intervals" and "sudden apparent recoveries." Her presentation was most often an attack of mania, including such symptom descriptions as "very noisy and talkative and destructive" (1876), "highly excited, talks vociferously" (1883), and "wild and excited and irrational in conversation" (1883). Less often she was described as depressed, and on one occasion she attempted suicide by drowning. There was little mention of interventions during these admissions, but those that were discussed included confinement in a "harness," "alternatives and tonics," "sulphoral," and work in the sewing room.

While the hospital records made no mention of it, the court commitment papers indicated that during Ms. A's sixteenth admission her father died. It was to his care that she had returned at each prior discharge. Ms. A's sixteenth hospitalization lasted 415 days, much longer than any prior stay. Her siblings, without their father, tried once to have her live at home. She was returned to Northampton State Hospital after 2 months for her seventeenth and last admission in 1886. With

no family to provide care for her in the community, she could not be discharged. She remained in Northampton State Hospital 10.4 years, demonstrating intermittent manic episodes during that decade. She died in the midst of one such episode. Her record ends: "She died of exhaustion."

Case 2. Ms. A's brother was a 27-year-old single man living at home when he was admitted for the first of 15 admissions to Northampton State Hospital in 1871. Like his sister, he had "recurrent mania," but unlike his sister he was often violent, sometimes ended up in jail, and often escaped from the hospital, only to be forcibly returned. His pattern of care paralleled that of Ms. A: short hospitalizations, followed by one much longer hospitalization after the father's death, one subsequent brief trial at home with the family, and then a final readmission lasting until his death in 1917.

Much in the psychiatric histories of this sister and brother sounds quite contemporary. They each had a chronic disease with acute exacerbations in a pattern recognized by modern researchers as the life course of untreated bipolar affective disorder (35). The family is an excellent case study of the genetic basis for the disorder; in fact, the cause of insanity listed in the records of both patients was "heredity." In a scenario that seems quite contemporary, the brother objected strenuously to being held at the state hospital against his will. In 1893 his record indicated, "Thinks it a great injustice for him to be allowed no chance to try life outside [the hospital]." The patients' histories of returning home to their father's care at each discharge, but no longer being able to be cared for and needing state hospital asylum once their father was deceased, presages by a century concerns and needs expressed by families who must care for relatives with chronic mental illness (36–38). Finally, Ms. A's and her brother's pattern of high numbers of admissions to the state hospital is remarkably contemporary; equally remarkable is how unusual it was in their time. They are the only two patients to have had 10 or more admissions for at least the first half-century that Northampton State Hospital was in operation.

DISCUSSION

At no time since the Asylum at Williamsburg opened its doors in 1773 as the first public hospital for the care and treatment of the mentally ill has it been harder to be admitted to a state hospital than in the last 15 years. But it is also true that at no time prior to the last 15 years have so many patients accumulated so many admissions. We are truly in the era of the revolving door.

There have been various contemporary explanations of the recidivism phenomenon, which this historical perspective refutes somewhat. Some authors have indicated that in the nineteenth century few persons were ever discharged, and the low rates of recidivism were simply an artifact of no potential candidates for readmission. For example, Ridgway and Zippel (39) stated, "If one were admitted to such an asylum and not dis-

charged rapidly, the institution often became one's 'home'. The data presented here indicate that persons were admitted, treated over periods of weeks to years, and discharged. The notion that few persons left nineteenth-century state hospitals alive is not supported by the Northampton State Hospital data.

Weinstein (40) has indicated that current recidivism rates are partly an artifact of changed regulations and procedures concerning "visit" or "convalescent" status; i.e., patients leave the hospital but remain on the books, so that their return to the hospital is not tabulated as a readmission. While "paroling" patients was not a common nineteenth-century practice, it was not unknown to the alienist of that era (41). The use of visit status was a common practice in the 1930s. However, if we use the same criteria as were used at Northampton State Hospital in the 1980s (visit status could be granted for up to 30 days' duration) and thereby convert returns from visits of over 30 days in 1936 to readmissions, we would increase the recidivism rate from 17.6% to 24.7%, or still only about one-third the 1980s repeat admission rate.

Weinstein (40) also accounted for the apparent readmission explosion by a decrease in the rate of first admissions. This is certainly the case, as shown in table 2. Great effort has gone into creating contemporary systems to divert admissions from public facilities to private alternatives (42). This is not, however, because of some new realization of the potential benefits of such diversion. Jarvis (43), in 1860, reported quite cogently on this practice: "For those insane patients who can be managed under personal influences and in proper circumstances, there are some advantages and privileges which can be enjoyed in a higher degree in private and discreetly managed houses than in public establishments" (p. 27).

As this review indicates, it is not a change in the clinical characteristics of patients, nor a change in the etiology of mental disorders, nor a change in contemporary beliefs in innovative clinical interventions, nor a change in therapeutic optimism, nor even a change in the moral dilemmas of providing care that accounts for the current phenomenon of state hospital recidivism. Rather, the role of the state hospital has been altered by factors extrinsic to both the provider and the recipient of psychiatric services. And the state hospital, as shown, has been profoundly altered. It is hoped that understanding the history of the state hospital will help us to chart its future better. Granted, many aspects of the functioning of state hospitals in the past have been questionable at best. But does the current role of the state hospital—in which society refuses to permit asylum to those who are unable to function without its succor while simultaneously condoning a system of care whereby some individuals are admitted more than 100 times—make any sense?

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Meta-Analysis of Subjective Sensitivity to Alcohol in Sons of Alcoholics

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***Objective:** Meta-analysis was used to review the research literature on self-reported sensitivity to alcohol among sons of alcoholic and among normal control subjects. **Method:** Computerized and manual searches identified 17 eligible independent articles; nine contained the information necessary to compute effect sizes, and additional data on two other studies were provided by authors in response to written and telephone requests. **Results:** Findings from 10 studies indicated that sons of alcoholics report significantly less sensitivity to alcohol than normal control subjects overall and during the ascending (i.e., 0–35 minutes after alcohol) and descending (i.e., 40–240 minutes after alcohol) limbs of the blood alcohol curve. Response to placebo did not significantly distinguish these groups in the five studies that included such assessment. **Conclusions:** It may be appropriate to apprise the biological sons of male alcoholics that they may experience less subjective sensitivity to alcohol than other individuals, but it is not possible to predict whether any particular individual will experience such lower sensitivity. In addition, self-report data can be influenced by many factors, and further research that assesses multiple psychological and physiological measures and uses longitudinal designs is needed to determine the relationship between specific factors and the development of alcoholism.*

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Sons of alcoholics are a group at high risk for developing alcoholism. In the past decade, multiple research studies have compared self-reported sensitivity to alcohol effects among sons of alcoholics and normal control subjects. Two differing theoretical perspectives have emerged from this research.

One theoretical perspective is that sensitivity to alcohol effects in sons of alcoholics varies depending on the blood alcohol curve (1). Under this view, sons of alcoholics exhibit greater than normal sensitivity to alcohol during the ascending limb, when its positive effects are purportedly greatest, and lower than normal sensitivity to it during the descending limb, when alcohol's negative effects are reportedly dominant. Thus, sons of alcoholics are vulnerable to developing alcoholism because the greater subjective sensitivity they possess during the ascending limb reinforces their drinking, and this is coupled with their relative imperviousness to alcohol's negative effects.

A second theoretical perspective is based on the premise that sons of alcoholics possess less subjective sensitivity to alcohol than do normal individuals (2). According to this view, sons of alcoholics are more vulnerable to developing alcoholism because they are less sensitive to alcohol effects after three to five drinks than are control subjects. Hence, they find it more difficult to regulate their alcohol consumption because they receive less internal feedback at these lower doses. Consequently, because they lack sensitivity to cues that normal subjects use to regulate drinking, sons of alcoholics are likely to consume more alcohol than do normal individuals within drinking sessions, and over time this contributes to the development of dependence.

In this study meta-analysis was used to review the empirical research literature on the self-reported sensitivity to alcohol of sons of alcoholics and of control subjects. Meta-analysis embodies a variety of techniques that quantitatively summarize the results of a number of individual studies designed to address a common theme or issue (3–5). Individual study outcomes in meta-analysis are usually represented by an effect size. Unlike statistical significance testing, in which the likelihood of group differences is inferred by using a binary decision strategy, the effect size provides an index of the magnitude of difference that distinguishes groups. Typically, the effect sizes culled from individual studies constitute the dependent variables examined in meta-analysis.

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Not all sons of alcoholics are likely to develop alcoholism themselves. The effect size and hence the statistical power based on comparisons of sons of alcoholics and normal control subjects are therefore likely to be less than those in studies in which pre-alcoholics are compared with normal subjects. Because low statistical power may account for the apparent divergence in some of the results reported to date, the aggregation of effect sizes by meta-analysis might prove especially helpful in assessing the overall consistency of findings in this research literature (e.g., 6).

In this report meta-analysis is used to evaluate hypotheses derived from each of the two theoretical perspectives already described. According to the first theoretical perspective, sons of alcoholics will report greater sensitivity to alcohol effects during the ascending limb of the blood alcohol curve than will normal control subjects but less sensitivity to it during the descending limb. According to the second theoretical perspective, sons of alcoholics will report less sensitivity to alcohol after alcohol ingestion than will control subjects.

METHOD

Identification of Studies

Two computerized literature searches, one on MEDLINE for 1985 through February 1991 and one on PsycINFO for 1984 through February 1991, were used to supplement the pool of published studies identified in prior reviews (1, 7). Manual searches of the reference sections of each review and individual study were performed to identify additional articles. Informal questioning of researchers in the area was used to locate relevant unpublished work.

Nineteen articles were identified. One (8) was eliminated because it evaluated women exclusively, and this meta-analysis assessed men. A second article (9) was excluded because the subject group consisted of a mixture of identical and fraternal twins and sibling pairs, and in this case it was not clear how to compute an effect size that could be meaningfully compared to those of the other studies. Thus, the total number of studies potentially available for the present meta-analysis was 17 (10–26).

In nine studies the information necessary to compute the effect sizes for between-group designs was available in the text or tables (13, 19–22, 25) or graphs (18, 23, 24). Letters requesting additional data were sent to the authors of some of these studies, and two responses were received. Specifically, Moss et al. (18) provided complete numeric data, so it was not necessary to estimate these values from the graphs. Vogel-Sprott and Chipperfield (25) provided data on four time points (30, 70, 80, and 130 minutes postalcohol), and this information was used in addition to the data for the 60-minute time point that were published in their article.

The eight remaining studies did not contain enough information to compute the effect sizes. Additional in-

formation was requested through a letter or telephone call to the primary author or the author identified as the correspondent in the published article (10–12, 14–17, 26). Of the responses received, two contributed data to this meta-analysis (10, 12).

In total, 11 independent research studies provided data for the present meta-analysis. The methods for assessing the subjects' self-ratings varied in these studies. In seven of them, the subjects' self-ratings of how "high" or "intoxicated" they were constituted the dependent variable selected for this meta-analysis (10, 12, 18, 20, 21, 23, 25). In two studies, the dependent variable was the subjects' self-ratings of how much the alcohol (19) or the drug (24) had affected them. In the two remaining studies, the total score on the Sensation Scale (13) or the score on the central stimulant subscale of the Sensation Scale (22) was used.

Effect Sizes

The effect size for each study was computed as the mean for the control group minus the mean for the group of sons of alcoholics divided by their pooled standard deviation (4, p. 78). Although some studies obtained self-ratings at baseline (i.e., before beverage administrations), frequently none of the subjects reported feeling affected by alcohol at this time point. Therefore, this time point was discarded from all analyses because virtually no effect sizes for it could be computed. For the remaining data, the number of effect sizes computed per study ranged from one (13) to 24 (three doses multiplied by eight time periods) (18).

Subgroups of subjects were examined in two studies. In both of them, effect sizes were computed as averages over subgroups, weighted by group size, so that all of the subjects' data examined in the original studies were represented. The rationale underlying this decision was to avoid biasing the meta-analysis results by failing to include all subjects. Thus, in one study in which the sons of alcoholics consisted of two subgroups—those with trans- versus unigenerational family histories of alcoholism (13)—the effect size computed was based on the weighted average of the two subgroups contrasted with the control subjects. In the other study, the four subgroups examined were sons of alcoholic and control subjects with and without antisocial personality disorder (10). These effect sizes were constructed by using a weighted average to compare subjects with and without family histories of alcoholism irrespective of antisocial personality disorder.

Plan of Analyses

Separate analyses were used to assess group differences under the alcohol and placebo conditions. All meta-analyses were based on studies weighted according to their group sizes (4).

First, an overall meta-analysis was used to assess differences between the self-reported sensitivity to alcohol of sons of alcoholics and that of control subjects. For

TABLE 1. Results of Meta-Analysis of Self-Reported Sensitivity to Alcohol in Sons of Alcoholics and in Normal Subjects

Study	d ^a	95% Confidence Interval	Subjects With Positive/Negative Family History	
			Positive	Negative
Alcohol sessions				
Bauer and Hesselbrock (10)	0.17	-0.27 to 0.61	36	46
de Wit and McCracken (12)	-0.06	-0.89 to 0.78	11	11
Finn and Pihl (13)	0.34	-0.36 to 1.04	24	12
Moss et al. (18)	0.18	-0.70 to 1.06	10	10
O'Malley and Maisto (20)	0.60	-0.11 to 1.31	16	16
Pollock et al. (21)	0.34	-0.19 to 0.86	34	24
Savoie et al. (22)	0.47	-0.69 to 1.64	5	7
Schuckit (23)	0.79	0.14 to 1.43	20	20
Schuckit (24)	0.50	-0.08 to 1.09	23	23
Vogel-Sprott and Chipperfield (25)	0.02	-0.75 to 0.79	13	13
Overall	0.34	0.13 to 0.55	192	182
Placebo sessions				
Bauer and Hesselbrock (10)	0.14	-0.29 to 0.58	36	45
de Wit and McCracken (12)	0.35	-0.49 to 1.19	11	11
Moss et al. (18)	0.23	-0.65 to 1.11	10	10
Newlin (19)	-0.62	-1.28 to 0.04	11	51
O'Malley and Maisto (20)	0.78	-0.23 to 1.80	8	8
Overall	0.08	-0.22 to 0.38	76	125

^aEffect size.

this comparison, one effect size per study was computed by averaging the effect sizes within single studies across time periods and alcohol doses. In addition, in a second set, separate analyses of two time periods following alcohol administration (time period 1: 0 to 35 minutes; time period 2: 40–240 minutes) were performed. Within each of these two time periods, multiple effect sizes per study were typically available. Again, the effect sizes used to represent the studies within each time period were obtained by averaging them across the relevant time periods and alcohol doses within studies. Once derived, the correction for bias described by Hedges and Olkin (4, p. 81) was applied to each effect size.

In some studies the control subjects did not differ in sex or age from the sons of alcoholics, whereas in others these groups were explicitly matched for sex and age, as well as other variables. The computation of effect sizes for within-group designs differs from that for between-group designs (27, p. 48), but none of the studies reported the information necessary to compute effect sizes for the former. Therefore, in the present study all effect sizes were computed by assuming between-group designs. The bias induced by this decision is likely to lead to underestimation of group differences (27) if, in fact, the within-group design reduces variance that is extraneous to the group comparisons.

The meta-analysis of the placebo sessions included the results reported in all relevant studies except for one in which reliable estimates of the effect size could not be obtained from the graph (24). A single effect size was used to represent each study in this meta-analysis. As already described, if data were acquired at multiple time periods, the effect sizes were averaged before the correction for bias was applied (4, p. 81).

RESULTS

Alcohol Sessions

Ten studies yielded information on the response to alcohol of 192 sons of alcoholics and 182 control subjects (table 1). The overall mean effect size of 0.34 is small to moderate (27). Its direction indicates that sons of alcoholics report less sensitivity to alcohol than do control subjects. The group difference is statistically significant in that the two-sided 95% confidence interval surrounding it excludes zero (i.e., 0.13 to 0.55).

To assess the hypotheses that sons of alcoholics exhibit greater than normal sensitivity to alcohol during the ascending limb but less sensitivity during the descending limb of the blood alcohol curve, separate mean effect sizes and confidence intervals were derived for the seven studies that obtained subjects' self-ratings 0 to 35 minutes after alcohol administration and for the 10 studies that obtained these data 40 to 240 minutes after alcohol. The results indicate that sons of alcoholics report significantly less sensitivity to alcohol than do normal subjects during both time periods: for 0–35 minutes the mean effect size was 0.32 and the two-sided 95% confidence interval was 0.07 to 0.56 (sons of alcoholics, $N=140$; control subjects, $N=140$), and for 40 to 240 minutes the mean effect size was 0.33 and the two-sided 95% confidence interval was 0.12 to 0.54 (sons of alcoholics, $N=184$; control subjects, $N=174$).

Placebo Sessions

Five studies yielded information on the response to placebo of 76 sons of alcoholics and 125 control subjects (table 1). The overall mean effect size of 0.08 is small.

Because its 95% confidence interval includes zero (i.e., -0.22 to 0.38), these results indicate that self-reported sensitivity to placebo does not significantly distinguish sons of alcoholics from control subjects.

DISCUSSION

The meta-analysis results indicate that sons of alcoholics report significantly less sensitivity to alcohol after alcohol ingestion than do normal control subjects. The sons of alcoholics' self-ratings of alcohol effects were significantly lower than those of control subjects during the ascending (i.e., 0–35 minutes after alcohol administration) and descending (i.e., 40 to 240 minutes after alcohol administration) limbs of the blood alcohol curve. The self-ratings obtained after placebo administration did not significantly distinguish sons of alcoholics from normal control subjects.

The meta-analysis findings clearly support the theoretical perspective that sons of alcoholics report less sensitivity to alcohol than do normal control subjects (2). These results provide no support and, in fact, contradict a hypothesis derived from an alternative theoretical view, which specifies that sons of alcoholics exhibit greater sensitivity to alcohol than control subjects during the ascending limb of the blood alcohol curve (1).

Multiple methodological moderators, such as the nature of the subject groups, between- versus within-group designs, differences in the methods of assessing subjective sensitivity, variations in the alcohol doses administered to subjects, and the time periods at which self-ratings were acquired, were not examined in this work. The influence of such factors can be evaluated by meta-analysis (3–5). However, because the present review was based on a small set of studies, it seems unlikely that meta-analytic evaluation of these methodological factors would yield stable results (28). Therefore, no such moderator analyses were undertaken.

Approximately two-thirds of all of the eligible studies identified (i.e., 11 of 17) contributed data to the meta-analysis. The possibility of bias in the meta-analysis results reported here due to the exclusion of six studies cannot be definitively discounted. Nonetheless, I attempted to obtain data for all studies and I have no reason to believe the 11 studies that provided the data are an unrepresentative subset.

Response to placebo failed to distinguish the sons of alcoholics from control subjects. This result, however, requires cautious interpretation because more studies obtained data in alcohol than in placebo conditions (i.e., 10 versus five, respectively). Consequently, the statistical power for detecting effects may have been greater for the alcohol condition. Within single empirical studies, placebo sessions are critical for assessing factors that might be important in understanding subjective responses to alcohol or other substances. Thus, the fact that the present meta-analysis failed to reveal a significant difference between the sons of alcoholics and control subjects in their responses to placebo

should not be used as a rationale to omit or discontinue placebo sessions in individual empirical research studies. Indeed, because of possible bias arising from subject and experimenter expectancy effects, results of placebo sessions are critical for interpretation of individual study results.

The mean effect size obtained in this meta-analysis can be used in conjunction with the specification of other design features to estimate the number of subjects that would be necessary to document statistically significant differences between sons of alcoholics and control groups in this type of research most of the time (i.e., power=0.80). By using a between-group design, a bidirectional significance test, and a type I error of 0.05 (i.e., $\alpha=0.05$), most of the time (i.e., power=0.80) comparisons of approximately 137 sons of alcoholics and 137 control subjects would be needed to demonstrate that sons of alcoholics exhibit less sensitivity to alcohol. These sample size estimates could, however, be lessened substantially if the error variance were reduced, as can sometimes be achieved by using a within-group design. If, for example, a within-group design in which the correlation between the matched groups' scores of 0.85 was used in conjunction with the design features already specified (i.e., power=0.80, bidirectional significance test with type I error of 0.05), then approximately 21 sons of alcoholics and 21 control subjects would provide a sample size sufficient to demonstrate these same group differences.

The results of this meta-analysis are consistent with the suggestion that it might be appropriate to apprise the biological sons of male alcoholics of the possibility that they may experience less subjective sensitivity to alcohol than other individuals. Specifically, these offspring could be informed that after consuming low to moderate doses of alcohol they might feel as though they are not as affected (or as "high" or intoxicated) as other individuals (see, for example, reference 24). Also, it might be appropriate to describe one possible way in which this risk factor could influence the development of alcoholism. That is, it could be explained that sons of alcoholics who report less subjective sensitivity to alcohol might be more likely to consume more alcohol than other individuals and that this might contribute to excessive alcohol use that leads to abuse or dependence. In addition to imparting such information, it should be emphasized that the limitations inherent in the present research studies make it impossible to predict whether any single individual will experience less sensitivity to alcohol or to specify who will develop alcoholism in the future.

The interpretation of the finding that sons of alcoholics report less sensitivity to alcohol than control subjects is not straightforward because self-report data can be influenced by many factors. For example, it is possible that the groups possess differential cognitive abilities which affect their proficiency in verbal communication or that group-related personality features mediated these findings (see reference 29 for review). Alternatively, the lower subjective sensitivity reported by sons

of alcoholics after consuming alcohol might reflect a genuine biologically mediated characteristic that distinguishes them from control subjects. This latter interpretation is supported by physiological data which suggest that sons of alcoholics manifest less intense responses to alcohol than do control subjects in terms of prolactin (30), cortisol (31), and P3 (32). Future research that incorporates multiple psychological and physiological measures is needed to assess these possibilities, even if the results are difficult to interpret because the results of studies based on multiple measures may not allow simple or straightforward interpretations.

Ultimately, the predictive validity of low subjective sensitivity to alcohol as a risk factor contributing to the development of alcoholism requires data from follow-up studies using longitudinal designs. Early results from a 10-year follow-up of sons of alcoholics and control subjects corroborate a relationship between a lower than normal reaction to alcohol and the future development of alcoholism (33). Thus, these preliminary findings attest to the etiological importance of subjective sensitivity to alcohol as a risk factor.

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Cross-Cultural Differences in Rating Hyperactive-Disruptive Behaviors in Children

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***Objective:** To determine the extent to which the reported variations across countries in the prevalence of attention-deficit hyperactivity disorder are due to cultural differences among raters, the authors examined the degree to which mental health professionals in four countries differed in their ratings of hyperactive-disruptive behaviors in children. **Method:** Mental health professionals from China (N=8), Indonesia (N=12), Japan (N=9), and the United States (N=8) rated the presence and degree of hyperactive-disruptive behaviors in standardized videotape vignettes of four 8-year-old boys participating in individual and group activities. **Results:** Chinese and Indonesian clinicians gave significantly higher scores for hyperactive-disruptive behaviors than did their Japanese and American colleagues. **Conclusions:** These findings suggest that perceptions of hyperactivity vary significantly across countries even if uniform rating criteria are applied. Without correction for these perceptual differences, cross-cultural prevalence rates of hyperactivity may not be comparable.*

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Wide variations across countries in the prevalence of attention-deficit hyperactivity disorder have been reported. In the United States 1%-12% of elementary school children are reportedly affected (1, 2). Surveys in England indicated a prevalence of less than 1% (3). To our knowledge, no hyperactivity was diagnosed in China before 1978 (unpublished 1977 paper by R.L. Sprague et al.), but since popularization of the concept, prevalence rates ranging from 2% to 13% have been published (4).

Most international prevalence data cannot be compared because diverse diagnostic criteria and assessment tools have been used. Application of comparable behavioral rating scales has partially reduced prevalence discrepancies in such countries as Australia, Germany, Great Britain, New Zealand, and the United States (5). However, the ways in which clinicians from

different countries use these rating systems continue to differ. For example, Prendergast et al. (6) reported that rigorous training in diagnostic categories improved but did not eliminate differences between U.S. and British research teams in assessing written case records and, in some instances, videotaped interviews for disruptive behavior disorders. Practicing clinicians in both countries showed significantly less concordance than researchers in their evaluations.

Such differences in clinicians' perceptions are likely to be even greater in comparisons of raters from countries with less similar cultural and historical backgrounds.

Because inattention, impulsivity, motor restlessness, and disruptiveness are found in all children to some degree, the diagnosis of attention-deficit hyperactivity disorder and other disruptive behavior disorders is based more on an assessment of developmentally inappropriate intensity, frequency, and/or duration of the behavior rather than its mere presence. Such judgments increase the possibility of observer bias. In particular, different culturally determined standards for normal behaviors may influence ratings of observed behaviors. Especially in nonpsychotic psychiatric illness, cultural background has been demonstrated to have a substantial influence on the interpretation of behavior as normal or pathological (7). This suggests that prevalence studies for any disorder should not be undertaken in the absence of prior knowledge about cross-cultural differences in the interpretation of the behaviors of interest.

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FIGURE 1. Checklist for Rating Disruptive Behaviors in Children Participating in Individual and Group Activities

	INDIVIDUAL				GROUP			
	0	1	2	3	0	1	2	3
	Not at All	Just a Little	Pretty Much	Very Much	Not at All	Just a Little	Pretty Much	Very Much
1. Fidgets with hands or feet or squirms in seat ^a								
2. Loses temper ^b								
3. Had difficulty remaining seated when required to do so ^a								
4. Is easily distracted by extraneous stimuli ^a								
5. Has difficulty sustaining attention in tasks or play activities ^a								
6. Shifts from one uncompleted activity to another ^a								
7. Excitable, impulsive ^c								
8. Talks excessively ^a								
9. Easily frustrated ^c								
10. Is angry and resentful ^b								
11. Had difficulty playing quietly ^a								
12. Swears or uses obscene language ^b								
13. Had difficulty awaiting turn in games or group situations ^a								
14. Deliberately does things that annoy other people, e.g., grabs other children's toys ^b								
15. Interrupts or intrudes on others, e.g., butts into other children's games ^a								
16. Does not seem to listen to what is being said to him or her ^a								
17. Initiates physical fights ^d								
18. Pushes or hits other children ^e								

INDIVIDUAL SCORE (1-12): _____ GROUP SCORE (1-18): _____

^aDerived from *DSM-III-R* criteria for attention-deficit hyperactivity disorder.

^bDerived from *DSM-III-R* criteria for oppositional defiant disorder.

^cDerived from Abbreviated Conners Teacher's Rating Scale.

^dDerived from *DSM-III-R* criteria for conduct disorder.

^eAdded by research team.

In planning for a standardized, cross-cultural prevalence survey of attention-deficit hyperactivity disorder in China, Indonesia, Japan, and the United States, we examined if and to what degree mental health professionals in the targeted countries differed in their ratings of hyperactive-disruptive behaviors.

METHOD

Videotape vignettes of four 8-year-old boys, two from Honolulu and two from Tokyo, were prepared under standardized conditions. The two boys at each site were selected from an outpatient clinic pool and a neighborhood elementary school, respectively. Since the purpose of the study was to examine the extent of rater differences in assessing observed behaviors, a diagnostic evaluation of the children was not required. However, children with marked physical handicaps, mental retardation, pervasive developmental deviations, or psychotic disorders were excluded. Each child was filmed alone and in a group. For the individual activity, the child was asked to sit at a table and draw a picture. He was told that he could play with any of the toys displayed in the video room as soon as he had completed his drawing. In the group activity, the child and two to three other male age mates were asked to build a block tower together. The children were told that they could play with any of the toys in the room after the tower fell over or was completed.

For each child, the videotapes were edited into an 8-10-minute segment with equal time for the individual and group activities. Through this editing, various degrees of targeted behaviors were emphasized, but extremes such as pervasive withdrawal or excessive aggressiveness were deleted.

An 18-item behavior observation checklist was developed (figure 1). Each item described a behavior that could be observed on the videotape without additional information about the child. All items except item 18 were directly derived from the *DSM-III-R* symptom checklist for disruptive behavior disorders (attention-deficit hyperactivity disorder, oppositional defiant disorder, conduct disorder) or the Abbreviated Conners Teacher's Rating Scale for hyperactivity (8).

Items from *DSM-III-R* and the Abbreviated Conners Teacher's Rating Scale were chosen because of the popular use of these instruments for rating and diagnosing disruptive behavior disorders in research. These rating systems have demonstrated positive psychometric qualities, including sensitivity, specificity, internal consistency (9), test-retest reliability (8), and convergent validity (10). Item 18 was added by the research team to specify physically aggressive acts.

Items 1-12 were to be rated for the child's solitary activity, and items 1-18 were rated for the group activity. Each item was rated on a 4-point scale ranging from 0 ("not at all") to 3 ("very much"). Therefore, the maximum attainable scores for individual and group

activities were 36 and 54, respectively. The behavior observation checklist was translated into Chinese, Indonesian, and Japanese and checked for accuracy through back-translation.

All of the raters were mental health professionals with experience in treating children. In China eight raters participated. Three were trained child psychiatrists, three were child psychiatry residents, and two were social workers. All but one had worked with children diagnosed as hyperactive. In Hawaii eight raters participated: four child psychiatrists, three child psychiatry residents, and one social worker. All had worked with children diagnosed as hyperactive. In Indonesia 12 raters participated: five child psychiatrists, five child psychiatry residents, one general psychiatry resident, and one psychologist. All but one had worked with children who were considered hyperactive. In Japan nine raters participated: two child psychiatrists, three general psychiatrists, three psychologists, and one social worker. All but two had worked with children diagnosed as hyperactive.

The videotapes were presented in the same order to all raters, who completed the behavior observation checklist immediately after each child's individual or group activity was shown.

Interrater reliability was assessed separately for the individual and group activity ratings. Overall mean scores for individual activity and group activity were analyzed by using separate split-plot analyses of variance.

RESULTS

Reliability Estimates

Intraclass correlation coefficients were calculated separately for the individual activity ratings and group activity ratings within the raters of each country (11). As shown in table 1, seven of the eight intraclass correlation coefficients were positive and substantial, indicating in these seven cases a satisfactory level of agreement among raters within any given country. The one negative value was strongly influenced by the great variation among the Chinese raters' group activity scores and relatively little variation across tapes.

Two more intraclass correlations were calculated to examine variation among the different countries for the individual and group activities. The intraclass correlation coefficients were 0.86 for the individual activity and 0.86 for the group activity, indicating that a high level of variance was accounted for by the rater's country of residence.

Between-Country Comparisons

Individual activity. A 4×4 (rater's country of residence and videotape) split-plot analysis of variance of the scores for the individual activity indicated significant main effects for rater's country of residence ($F=18.30$, $df=3, 32$, $p<0.001$) and for videotape ($F=19.40$,

TABLE 1. Intraclass Correlations and Means of Ratings of Disruptive Behavior by Mental Health Professionals in Four Countries Based on Videotapes of Four 8-Year-Old Boys in Individual and Group Activities^a

Videotape and Country of Rater	Intraclass Correlation Coefficient ^b	Rating ^c	
		Mean	SD
Individual activity			
China	0.44	19.5 _a	5.4
Indonesia	0.63	16.2 _a	6.9
United States	0.61	8.6 _b	5.5
Japan	0.43	7.4 _b	4.9
Group activity			
China	-0.44	24.8 _x	9.8
Indonesia	0.62	18.3 _y	6.9
United States	0.40	12.8 _z	6.7
Japan	0.47	11.7 _z	7.3

^aThe numbers of raters were as follows: China, N=8; Indonesia, N=12; United States, N=8; Japan, N=9.

^bStatistical logic and calculation procedures according to Bartko and Carpenter (11).

^cMeans with different subscripts are significantly different ($p<0.05$, Scheffé test).

$df=3, 96$, $p<0.001$). The interaction between rater's country and tape was nonsignificant ($F=1.01$, $df=9, 96$, $p>0.40$).

As shown in table 1, the mental health professionals from China and Indonesia made significantly higher ratings than the professionals from Japan and the United States ($p<0.05$ in all cases, according to the Scheffé test).

Tests of the main effect for videotape indicated that one tape significantly differed from the other three ($p<0.05$, Scheffé test). These differences, along with the absence of any interaction between rater and tape, confirm that a relatively broad range of disruptive behaviors were depicted in the videotapes and that the effects related to rater's country of residence were independent of these videotape characteristics. In fact, the pattern depicted in table 1 held for all four videotapes independently, further attesting to the generality of these statistical differences.

Group activity. A 4×4 (rater's country of residence and videotape) split-plot analysis of variance was also conducted on the scores for the group activity. Again, the results indicated main effects for rater's country of residence ($F=8.61$, $df=3, 32$, $p<0.001$) and for videotape ($F=10.36$, $df=3, 96$, $p<0.001$), whereas the interaction was nonsignificant ($F=0.85$, $df=9, 96$, $p>0.50$).

Further examination of the main effect for rater's country of residence by using Scheffé tests demonstrated that the mental health professionals from China made significantly higher ratings than did the professionals from Indonesia, who in turn gave higher ratings than American or Japanese raters (all $p<0.05$) (table 1).

As with the individual activity scores, the main effect for videotape on the group activity scores indicated a wide range of symptom levels. Again, country of residence had a clear and independent effect across all videotapes.

DISCUSSION

The results from the present study show substantive and reliable differences in ratings of hyperactive-disruptive behaviors in children among mental health professionals from four different countries. Specifically, clinicians from China and Indonesia rated target behaviors for all children higher than did clinicians from the United States and Japan. Since all raters observed identical tapes, the disparities are more likely due to differences in perception than to any differences in actual symptom level. This may reflect different cultural standards for appropriate childhood behaviors. For example, in China emotional control and conformity are valued and expected from preschool on, permissiveness and student self-regulation with little direct teacher discipline is characteristic for the lower school grades in Japan, and individual expression and creativity are emphasized in the United States (12).

Significant differences in cultural perceptions of symptoms may complicate comparisons of epidemiological studies of disruptive behavior disorders in different countries, especially if rating scales and behavioral observation are used as primary diagnostic tools. For example, even though the prevalence rates of attention-deficit hyperactivity disorder in China are reportedly similar to those in the United States (13), it remains unclear whether boys considered hyperactive in China would be diagnosed as hyperactive in the United States or Japan.

Any cross-cultural epidemiological study of disruptive behavior disorders, particularly attention-deficit hyperactivity disorder, which is diagnosed in terms of dimensional rather than categorical symptoms, will need to address the issue of perceptual differences in symptom interpretation.

While this study demonstrated significant cross-cultural variations in the perception of disruptive childhood behaviors, it did not assess whether higher scores were related to determining pathology and need for treatment. Such research should be done. Future research also should compare ratings of parents and other professionals—such as teachers and pediatricians, who frequently assess children's behaviors—in different countries. Specific symptoms should be analyzed to distinguish between those which seem to be universally perceived and those which are more culturally dependent. By building this data base, future epidemiological research will become more interpretable.

Finally, combining approaches that examine the meaning of the disruptive child within each culture with approaches that train mental health diagnosticians in different countries to effectively use universal, standardized criteria may be a useful method for achieving greater comparability of data (11, 14). The formation of cross-cultural diagnostic research teams might aid in this process.

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Deterioration in Premorbid Functioning in Schizophrenia: A Developmental Model of Negative Symptoms in Drug-Free Patients

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Objective: The authors examined the relationship between negative symptoms and premorbid variables in drug-free schizophrenic patients. **Method:** The authors studied 63 clinically stable male schizophrenic inpatients who were not receiving any psychoactive medication. The patients were classified as having negative, positive, or mixed symptoms, and their premorbid functioning during childhood, early adolescence, and late adolescence was assessed by using the Premorbid Adjustment Scale. Correlational analyses were applied to the classification and developmental models. **Results:** Patients with negative symptoms had significantly lower levels of premorbid functioning during late adolescence and significantly greater premorbid deterioration between childhood and early adolescence. Correlational analysis revealed significant positive relationships between premorbid variables and negative symptoms. **Conclusions:** The data suggest that a deterioration in social and intellectual functioning between childhood and adolescence is associated with the development of a negative symptom syndrome in schizophrenia. The premorbid deterioration appears to be an early prodrome of the disorder. Whether this residual negative symptom syndrome is in some way related to the deficit syndrome of schizophrenia awaits a prospective study.
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In the study of schizophrenia, much emphasis has been placed on subtyping in order to predict outcome and response to neuroleptic treatment. In 1980, Crow proposed the negative symptom syndrome of schizophrenia (1). Negative symptoms were thought to be nonresponsive to medications (2) and persistent over time (3, 4), suggesting a chronic condition. However, some negative symptoms have been shown to be state dependent in that they are drug responsive (4-7), increase with psychotic relapse (8, 9), and increase with drug withdrawal (10). In addition, negative symptoms have been found to respond to amphetamine administration (11). There is also an indication that negative symptoms can be the result of understimulation in the patient's social environment and are therefore reduced by behavioral intervention (12).

Some of these apparently conflicting findings may be

the result of an unclear definition of negative symptoms. Although some investigators proposed that poor social functioning and attentional impairment may be considered negative symptoms (13), Crow (14) suggested limiting the definition to flattening of affect and poverty of speech only. The specificity of negative symptoms to schizophrenia has also been questioned (15).

Carpenter et al. (16) attempted to solve this issue by making a distinction between deficit and nondeficit syndromes. In this paradigm the severity and persistence of symptoms are more important than the definition of symptoms; consistent negative symptoms that are not caused by depression, anxiety, medication effects, or environmental deprivation must be present for a period of at least 1 year. Symptoms are considered consistent if they show no response to neuroleptic treatment and do not lessen with remission of psychotic symptoms (16).

Explorations of negative symptoms led to the investigation of their relationship to poor premorbid social adjustment, which had been found to be correlated with several other negative variables such as poor outcome (17), poor drug response (18, 19), and CT scan abnormalities (20). Andreasen and Olsen (21) used a classification model (groups with positive, negative, and mixed symptoms) and showed that premorbid adjustment measured by the Phillips Scale (22) was significantly poorer in the group with negative symptoms.

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Andreasen et al. (23) replicated this finding in a more recent sample. Pogue-Geile and Harrow (3) reported a significant relationship between a fair or poor rating (lack of close friends, small number of acquaintances) of premorbid functioning and a negative symptom score. Davis and DeWolfe (24) reported a significant relationship between poor premorbid scores on the Phillips Scale and flattened affect measured by high scores on the MMPI psychasthenia scale (signifying inhibition of physical activity). Buchanan et al. (25) showed that poor premorbid functioning was also a component of the deficit syndrome (16). Not all studies have observed this relationship, however (2).

The Premorbid Adjustment Scale (26), introduced by Cannon-Spoor et al. in 1982, separated premorbid functioning into distinct life periods (childhood, early adolescence, late adolescence, and adulthood), which allows for an analysis of the developmental aspects of premorbid functioning. In their original assessment of schizophrenic patients (26), Cannon-Spoor et al. found a progressive deterioration in functioning through childhood, early adolescence, and late adolescence, with mean scores of 0.35, 0.44, and 0.52, respectively. This apparent deterioration in functioning suggested that negative symptoms could be studied in relation to a premorbid developmental model. Furthermore, the Premorbid Adjustment Scale rates both social and intellectual functioning; therefore, different aspects of premorbid functioning can be examined separately (27). Buchanan et al. (25) used this scale in their evaluation of aspects of the deficit syndrome.

Recently, Mukherjee et al. (27) proposed a premorbid developmental model for negative symptoms based on the Premorbid Adjustment Scale. Mukherjee et al. found evidence that the deterioration of functioning between childhood and early adolescence correlated with ratings of negative symptoms. Their study as well as many previous studies evaluated patients who were receiving medication. However, because negative symptoms can be drug responsive as well as drug induced (7, 11, 28), an evaluation of negative symptoms in drug-free subjects, without the complication of a psychotic exacerbation, may be a paradigm of residual negative symptoms that can be used to test this developmental hypothesis. In addition, evaluation of drug-free subjects is preferred due to the fact that patients with poor premorbid functioning may be given higher doses due to treatment resistance (18, 29), thus creating a systematic bias.

In the present study, we used negative symptom data from drug-free patients involved in our double-blind haloperidol withdrawal study (8). The data were analyzed by using correlational analyses as well as a modification of the classification approach of Andreasen et al. (23) to study the relationship between a premorbid decrease in adaptive functioning and the presence of negative symptoms in drug-free schizophrenic patients. The correlational analyses were used to address the issue of whether a negative syndrome is better studied as a category or as a continuous dimension (30).

METHOD

Subjects

The subjects were 63 male veterans admitted to our schizophrenia research unit. All of these patients had a *DSM-III-R* diagnosis of schizophrenia ($N=55$) or schizoaffective disorder ($N=8$). Information for the diagnosis was obtained by using the Schedule for Affective Disorders and Schizophrenia—Lifetime Version (31) as well as past medical records and contacts with the patient's family if possible. All diagnostic information was reviewed in a multidisciplinary case conference, and a consensus diagnosis was obtained. Fifty-three of the patients participated in a double-blind protocol that consisted of the replacement of long-term antipsychotic drug treatment with a stabilization period of haloperidol administration. If the patient had received a decanoate injection, he was not considered stable unless he had taken only oral haloperidol for at least 3 months. After the stabilization period, the unmarked haloperidol capsules were replaced by placebo capsules for up to 6 weeks. Another 10 clinically stable patients received a double-blind placebo trial on admission; these patients showed no recent psychotic exacerbation, although they may have been symptomatic at the time.

The mean age at the time of study of the 63 patients was 34.9 years ($SD=8.3$). Their mean age at first onset of psychotic symptoms was 22.9 years ($SD=4.8$). They had been ill with schizophrenia for a mean of 12.0 years ($SD=7.3$). Their mean number of years of formal education was 12.0 ($SD=1.8$).

Measures

Premorbid functioning was assessed by using the Premorbid Adjustment Scale (26); the scores were based on extensive information from the patient, the patient's family, and previous records. Data on the late adolescent period were not available for two patients because they developed schizophrenia before reaching this age period. Change scores were computed by subtracting the patients' childhood scores from their early adolescence scores (27). Because of the noticeable effect of the features of their illness on the adult premorbid scores, only the first three life periods were used for this analysis.

Although data for this scale have ordinarily been presented as percentages, reporting means gives the benefit of being able to refer to the 7-point scale measurement (0–6=normal–severely impaired) to assess the relationships between groups. (Percentage scores comparable to those in the previous literature can be computed by dividing the values presented by 6, the highest possible score.)

The Scale for the Assessment of Negative Symptoms (13) and the withdrawal cluster of the Brief Psychiatric Rating Scale (BPRS) (32) were used to assess negative symptoms. Positive symptoms were assessed for classification purposes by using the BPRS psychosis items

TABLE 1. Demographic and Clinical Characteristics of 63 Drug-Free Male Schizophrenic Inpatients With Positive, Mixed, or Negative Symptoms

Characteristic	Positive Symptoms (N=23)		Mixed Symptoms (N=28)		Negative Symptoms (N=12)		Analysis of Variance		
	Mean	SD	Mean	SD	Mean	SD	F	df	p ^a
Age at time of study (years)	34.2	6.2	35.1	10.2	35.5	7.6	0.13	2, 60	n.s.
Age at onset of first psychotic symptoms (years)	22.2	3.7	23.6	5.4	22.6	5.4	0.55	2, 60	n.s.
Duration of illness (years)	12.0	6.6	11.6	8.3	13.0	6.7	0.15	2, 60	n.s.
Formal education (years)	11.7	1.4	12.3	2.0	11.8	1.8	0.84	2, 60	n.s.
Scores on the Premorbid Adjustment Scale ^b									
Childhood	2.3	0.9	2.4	0.8	2.5	1.3	0.32	2, 60	n.s.
Early adolescence	2.5	1.1	2.6	1.1	3.4	1.4	2.68	2, 60	0.08
Late adolescence	2.6	1.0	2.8	1.2	3.8	1.5	3.81	2, 58	0.03
Premorbid deterioration ^c	0.2	0.6	0.2	0.6	0.8	1.3	3.25	2, 60	0.05

^an.s.=p>0.10.^bHigher scores indicate poorer functioning.^cEarly adolescence score on the Premorbid Adjustment Scale minus childhood score on the Premorbid Adjustment Scale.

that most closely corresponded to the positive criteria of Andreasen et al. (23)—1) hallucinatory behavior, 2) suspiciousness (i.e., delusional behavior), 3) conceptual disorganization/disorganized speech, and 4) unusual thought content and grandiosity. Because the strict application of Andreasen's negative symptom criteria resulted in classifying only three patients as having negative symptoms, we increased the sensitivity of the classification to our sample by extending the criterion to include a score of 3, indicating moderate negative symptoms. The final classification resulted in 12 patients with negative symptoms, 23 with positive symptoms, and 28 with mixed symptoms. None of the patients in the group with negative symptoms had a schizoaffective diagnosis.

Negative symptom ratings were done weekly by therapists blind to medication status; the ratings used for this study were taken after at least 2 weeks into the drug-free period in an attempt to eliminate the effects of drug withdrawal on the ratings. To avoid the confound of a psychotic relapse during the 2–6-week drug-free period, negative symptom ratings made when the patient's psychosis score was less than 2 points higher than his baseline psychosis score (determined while he was receiving haloperidol) were chosen. The psychosis score was determined on a 15-point global rating scale (33).

To maintain interrater reliability, interview sessions were held weekly; after the rating session, the therapists examined the discrepancies and discussed them. The data from these sessions were compiled every 6 months, and intraclass correlation coefficients were computed for all the items.

Statistics

For the first analysis, multivariate analysis of variance (ANOVA) was used to assess group differences in all premorbid adjustment variables (childhood, early adolescence, and late adolescence). Similarly, univariate ANOVA was used to assess the differences in demographic and premorbid deterioration variables across groups.

For the second analysis, Pearson correlational analyses were performed on the premorbid adjustment items and negative symptoms as well as a resultant negative factor score obtained from principal components analysis.

RESULTS

No differences in age at the time of the study, age at first onset of psychotic symptoms, duration of illness, or number of years of formal education were found among the patients with negative, positive, and mixed symptoms (table 1). Fifty-nine patients remained drug free for a mean of 33.0 days (SD=13.6); four patients never received drugs.

First Analysis

An ANOVA on the premorbid deterioration variable (early adolescence Premorbid Adjustment Scale score minus childhood score) indicated that the change in overall functioning between childhood and early adolescence was significantly different among groups and that the subjects with negative symptoms exhibited the most deterioration (table 1).

Because the univariate tests indicated a distinct pattern of deterioration, multivariate ANOVA using the three life periods as dependent variables was performed to test the hypothesis that the combination of these variables may provide additional support for the developmental model. This analysis did not reveal a significant main effect for Group (Hotelling's $T=0.194$, $F=1.78$, $p=0.11$).

Second Analysis

The results of Pearson correlation analyses are presented in table 2. It is interesting to note that avolition-apathy, anhedonia-asociality, and emotional withdrawal did not correlate with premorbid adjustment items. The same pattern of deterioration noted in the classification analysis was observed.

TABLE 2. Correlations Between Premorbid Functioning and Negative Symptoms in 63 Drug-Free Male Schizophrenic Inpatients With Positive, Mixed, or Negative Symptoms

Test of Schizophrenic Symptoms	Correlation With Score on Premorbid Adjustment Scale							
	Childhood		Early Adolescence		Late Adolescence ^a		Premorbid Deterioration ^b	
	r	p ^c	r	p ^c	r	p ^c	r	p ^c
Scale for the Assessment of Negative Symptoms								
Affective flattening	0.13	n.s.	0.26	0.04	0.28	0.03	0.24	0.06
Alogia	0.15	n.s.	0.31	0.02	0.28	0.03	0.28	0.03
Avolition-apathy	0.01	n.s.	0.11	n.s.	0.16	n.s.	0.15	n.s.
Anhedonia-asociality	-0.08	n.s.	0.05	n.s.	0.07	n.s.	0.17	n.s.
Attentional impairment	0.29	0.02	0.36	0.004	0.37	0.004	0.18	n.s.
BPRS								
Emotional withdrawal	0.06	n.s.	0.16	n.s.	0.18	n.s.	0.16	n.s.
Motor retardation	0.21	n.s.	0.46	0.0005	0.50	0.0005	0.42	0.001
Blunted affect	0.20	n.s.	0.31	0.01	0.34	0.007	0.22	n.s.

^aData are missing for two patients because their onset of schizophrenia occurred before late adolescence.

^bEarly adolescence score on the Premorbid Adjustment Scale minus childhood score on the Premorbid Adjustment Scale.

^cn.s.= $p > 0.10$.

Because the number of correlations inhibited the interpretation of these findings, we performed a data reduction using principal components analysis (varimax rotation), which resulted in a single factor score with the following component loadings: affective flattening, 0.852; blunted affect, 0.789; alogia, 0.785; emotional withdrawal, 0.769; anhedonia-asociality, 0.748; avolition-apathy, 0.717; motor retardation, 0.700; and attentional impairment, 0.611. The single factor explained 56.1% of the total variance. The correlation with this factor in childhood was $r=0.16$ ($N=63$, n.s.); in early adolescence, $r=0.33$ ($N=63$, $p=0.008$); in late adolescence, $r=0.35$ ($N=61$, $p=0.005$). (Data were missing for two patients in late adolescence because onset of schizophrenia occurred before late adolescence.) The correlation with premorbid deterioration was $r=0.30$ ($N=63$, $p=0.02$). The data reduction was successful in replicating and improving the relationships.

Additional Analyses

Although the patients were rated when clinically stable, the relationships between premorbid variables and other items of the BPRS were explored to ensure the specificity of the relationship between premorbid variables and negative symptoms. No significant relationships were found between premorbid variables and positive symptoms or depression (all p values were greater than 0.50). In addition, the analyses were performed without the eight patients with schizoaffective disorder to determine if including these patients significantly altered the relationships; no differences in the results were noted.

DISCUSSION

Our data indicate that the associations between premorbid functioning and negative symptoms found in

the previous literature (3, 25) remain significant when the effects of medication, relapse, and medication withdrawal are removed. Similarly, because we evaluated medication-free patients following withdrawal from chronic neuroleptic treatment, we found support for the association between poor premorbid functioning and a residual negative symptom syndrome, which may consist of deficit symptoms that persist independent from medication effects (16).

In evaluating premorbid functioning, it is necessary to establish whether poor functioning is an early manifestation of the illness itself or a particular vulnerability characteristic that assists in determining development of the illness, outcome, or symptomatology. The associations between premorbid functioning and negative symptoms found in this study as well as others (34) support either conclusion. However, our data particularly support those of Mukherjee et al. (27), who found that a deterioration in functioning between the periods of childhood and early adolescence was associated with the later presence of negative symptoms. This deterioration in functioning between childhood and early adolescence may be related to late maturation (35), altered myelination processes during late adolescence (36), and the hypothesized faulty synaptic pruning during adolescence (37-39) in schizophrenic patients. Buchanan et al. (25), in their study of the deficit syndrome, observed a similar pattern; differences between subgroups in premorbid functioning became increasingly significant from childhood onward, and the most significant difference occurred in late adolescence ($p=0.008$). This indicates that for some patients, particularly those who will manifest a negative syndrome later on, deterioration in premorbid functioning may represent the onset of the disorder.

Because we found that premorbid variables did not correlate with positive symptoms, it appears that the relationship to deterioration in premorbid functioning is specific to negative symptoms and not schizophrenic

pathology as a whole. Some authors have proposed that negative symptoms may be the more fundamental symptoms of schizophrenia (40) because they show more internal consistency (41). The relationship between premorbid deterioration and severity of negative symptoms supports this conclusion, if we assume that the deterioration in functioning represents an early prodrome of the disorder. It is conceivable that patients with premorbid deterioration have a more gradual onset than those with good premorbid functioning, who may have a more acute onset; this would have to be pursued in a prospective longitudinal design (42) rather than a retrospective cross-sectional study such as this.

A limitation of our study is that all of our subjects were men. Male schizophrenic patients have been shown to have poorer premorbid functioning (43, 44) and poorer treatment response (29, 45, 46) than female schizophrenic patients. There is also an indication that men have more negative symptoms, although this has been difficult to show empirically (34). In addition, it has been proposed that schizophrenia may be the result of a neurodevelopmental disorder and that the prevalence of these disorders are more common in men than women (47, 48). Thus, the relationships we found with the deterioration factor may not have been significant if female patients had been included in the study group. What role these neurodevelopmental abnormalities play in the deterioration of social and intellectual functioning is not fully understood. However, the concurrence of these phenomena is of interest and should be pursued further in a study group consisting of both sexes.

Premorbid functioning and deterioration were correlated significantly with all aspects of negative symptoms except anhedonia-asociality, avolition-apathy, and emotional withdrawal, suggesting that some of these symptoms may be in response to the illness itself. This supports the more restricted definition of negative symptoms suggested by Crow (14), indicating that the only true negative symptoms are those we can distinguish from depression or the side effects of positive symptoms. This finding is particularly interesting because our stability criterion may have eliminated secondary exacerbation effects, thus illuminating this relationship. Further, our inpatient milieu may provide the necessary environmental intervention needed to avoid the confounding effects of lack of stimulation on the negative symptom ratings (12). These aspects of the present study may have controlled some of the variance in negative symptoms and thus strengthen the interpretation of the relationships. Our data indicate that the patients' clinical status and longitudinal observations are important in the assessment of these relationships in studies of negative and positive symptoms.

Our subtyping model exhibited similar relationships to the correlational model, indicating that although viewing negative symptoms as a continuum of pathology is certainly warranted, meaningful subtypes do exist under well-defined clinical conditions such as those in this study. The present data and the deficit versus

nondeficit distinction (16) as well as the Kraepelinian subtype of schizophrenia, which represents severe dysfunction in employment and self-care capabilities (49), suggest that the negative dimension is meaningful in determining diagnosis, treatment, and outcome. Although a cross-sectional evaluation of drug-free patients does give an insight into how residual negative symptoms are, it does not argue that the negative subtype exists longitudinally (4). As such, the significance observed between these subtypes may be an artifact of cross-sectional rather than longitudinal types of analyses (42). Clearly, most of the patients in our study group as well as others (23) have mixed symptoms. However, under these well-defined conditions the dichotomy between positive and negative symptoms provides some insight into the nature and perhaps the origin of the disorder in this group of patients that can be used in future longitudinal studies.

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Technique for Training Schizophrenic Patients in Illness Self-Management: A Controlled Trial

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Objective: To determine whether schizophrenic outpatients receiving low-dose neuroleptic therapy could learn and retain complex information and skills related to self-management of their illness, a novel technique of teaching, using cognitive and behavioral methods, was designed to compensate for the patients' learning disabilities. **Method:** The subjects were 41 patients with DSM-III-R schizophrenia who were receiving constant maintenance neuroleptic drug therapy. They were randomly assigned to structured, modularized skills training or to supportive group psychotherapy. **Results:** The patients who received skills training made significant gains in each of the areas taught, while those participating in group therapy did not. The skills learned during training were retained without significant erosion over a 1-year follow-up period. **Conclusions:** The effectiveness of modularized teaching of illness self-management skills to schizophrenic patients appears to be largely independent of baseline psychopathology and symptom improvement. Such an approach is useful for overcoming or compensating for the enduring cognitive and information processing deficits commonly found in schizophrenia.

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The public health problems posed by schizophrenia, as well as the personal misery experienced by patients and their families, are amplified by the "revolving door" pattern of multiple rehospitalizations and homelessness, which are so often the consequences of patients' failing to adhere to their treatment regimens (1, 2). Despite more than a quarter century of research evidence for the efficacy of maintenance neuroleptic therapy in reducing relapse rates for patients with chronic schizophrenia, reliable compliance with medication is more the exception than the rule (3, 4).

Consistent with the current emphasis on promoting patients' understanding of their illness and cooperation

with their treatment, skills training has emerged in recent years as an effective technique for psychiatric rehabilitation (5). As a psychosocial adjunct to antipsychotic drug therapy, training schizophrenic patients in social and independent living skills—through individual, group, and family therapies—has yielded improvements in social functioning, reductions in relapse rates, and superior cost-effectiveness (6-9). However, there are considerable obstacles to the generalized use of skills training in schizophrenia and to its specific application to improving patients' grasp of such complex behaviors as monitoring medication effects and identifying prodromal symptoms of relapse. Foremost among the obstacles are the intrusion of persisting and intercurrent symptoms into the learning process (10) and the enduring cognitive deficits that appear to be vulnerability markers in schizophrenia (11). For example, deficits in sustained attention, memory, and executive functioning impair the information processing required for learning complex knowledge and skills (12).

If skills training is to be effective in teaching patients how to be more responsible and reliable consumers of treatment, the training procedures must be designed to overcome or compensate for the enduring cognitive and information processing deficits commonly found in schizophrenia. Furthermore, the training techniques must include ways to overcome the negative symptoms

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TABLE 1. Characteristics of Schizophrenic Patients Randomly Assigned to Skills Training (N=20) or Group Psychotherapy (N=21)

Characteristic	Skills Training		Group Psychotherapy	
	Mean	SD	Mean	SD
Age (years)	40.90	9.39	38.67	7.93
Duration of illness (months)	171.50	110.16	165.24	86.21
Age at onset of illness (years)	26.10	7.07	24.76	4.92
Number of hospitalizations	3.75	2.27	4.00	1.61
Highest grade completed ^a	12.15	1.76	13.57	1.54

^at=2.76, df=39, p=0.009.

of schizophrenia, including anhedonia, blunted affect, social withdrawal, lack of motivation, anergia, poverty of speech, and depression (13). A modular form of training in social and independent living skills, designed to counter the symptomatic and cognitive barriers to learning, has been developed by the UCLA Clinical Research Center for Schizophrenia and Psychiatric Rehabilitation and has been field tested in facilities throughout the United States and Canada (14). The present controlled clinical trial examined the efficacy of these modules in teaching skills involved in symptom and medication self-management to schizophrenic outpatients maintained on a low-dose neuroleptic drug regimen.

METHOD

Subjects

The study group was composed of 41 male veterans who met the *DSM-III-R* criteria for schizophrenia according to diagnostic interviews using the Present State Examination to elicit signs and symptoms. Most subjects had had 10 or more years of treatment for schizophrenia and were recruited from inpatient and outpatient units of a U.S. Department of Veterans Affairs hospital. Their mean age was 40 (SD=8.6), and only 27% (N=11) had ever been married. On average, they had 13 years (SD=1.8) of education. Of the 40 subjects for whom ethnic data were available, 14 (35%) were Caucasian, 23 (58%) were black, and three (8%) were Hispanic. Of the 20 patients randomly assigned to skills training, 16 (80%) were unemployed during the entire prior year, compared with 11 (52%) of the 21 patients who received group psychotherapy; this difference was not significant. Other characteristics of the subjects assigned to the two psychosocial treatment conditions are listed in table 1. While the subjects assigned to supportive group therapy had, on average, 13.57 years of education and those assigned to social skills training had an average of 12.15 years, the other variables showed no statistically significant differences between treatment groups.

To qualify for entry into the study, subjects were required to have no evidence of mental retardation or organic brain syndrome, to not be currently abusing alcohol or drugs (as determined by urine toxicologic test-

ing), and to be able to tolerate 5–10 mg of fluphenazine decanoate every other week. This study was nested within a larger project examining the effects of lower than conventional doses of neuroleptic medication. The 41 subjects who participated in the study reported here were those who completed at least 6 months of psychosocial treatment and the full battery of pre- and post-treatment assessments.

Experimental Design

Upon entry into the study, each patient was randomly assigned to either skills training in groups or to supportive group psychotherapy. The subjects were carefully monitored on a weekly basis over the 18-month study period for indications of clinical instability, prodromal symptoms, or exacerbations of their disorder. Depending on their clinical states, the subjects received time-limited oral fluphenazine or placebo supplementation of their 5–10-mg biweekly fluphenazine decanoate until the prodrome or exacerbated state was controlled. Over the course of the 18 months there was no significant difference in cumulative fluphenazine dose between the subjects receiving skills training and those receiving group therapy.

The study was a repeated measures design comparing two psychosocial interventions at four time intervals—pretreatment baseline, posttreatment, and 6- and 12-month follow-ups. In addition to the designated psychosocial treatments (to be described), all subjects received case management, psychiatric services, and ancillary medical and social services as needed in the research outpatient clinic of the hospital. The subjects attended the clinic at least biweekly, receiving their depot injections and clinical status evaluations from the clinic nurse, social worker, and psychiatrists.

Treatments

Group psychotherapy. These subjects engaged in an insight-oriented and supportive group process that was leavened with abundant information and education about schizophrenia as an illness and the importance of adhering to prescribed treatments. While of necessity there was discussion of medication and symptom management, no structured curriculum was followed and no formal behavioral techniques were used. The group could be best described as aiming for individual and personal goals encouraged through exploratory and supportive leadership. The group was led by a psychologist with more than 6 years of experience in leading therapy groups of patients with chronic schizophrenia. During twice-weekly 90-minute sessions, the group members discussed problems encountered in daily living and in their social relationships. Mutual understanding, social support, and group cohesion were emphasized. The subjects were encouraged to offer suggestions and explore solutions to the problems raised by one another. The therapist used customary group therapy techniques, such as open-ended questions, re-

TABLE 2. Skill Areas and Learning Objectives in the Medication Management and Symptom Management Modules of the UCLA Social and Independent Living Skills Program

Module	Skill Areas	Learning Objectives
Symptom management	Identifying warning signs of relapse	To identify personal warning signs
	Managing warning signs	To monitor personal warning signs with assistance from other people To obtain assistance from health care providers in differentiating personal warning signs from persistent symptoms, medication side effects, and variations in mood; to develop an emergency plan for responding to warning signs
	Coping with persistent symptoms	To recognize and monitor persistent personal symptoms; to obtain assistance from health care providers in differentiating persistent symptoms from warning signs, medication side effects, and variations in mood; to use specific techniques for coping with persistent symptoms
	Avoiding alcohol and street drugs	To monitor persistent symptoms daily To identify the adverse effects of alcohol and illicit drugs and the benefits of avoiding them; to refuse offers of alcohol and street drugs; to know how to resist using these substances in coping with anxiety, low self-esteem, or depression; to discuss openly use of alcohol and drugs with health care providers
Medication management	Obtaining information about antipsychotic medication	To understand how these drugs work, why maintenance drug therapy is used, and the benefits of taking medication
	Knowing correct self-administration and evaluation	To follow the appropriate procedures for taking medication; to evaluate responses to medication daily
	Identifying side effects of medication	To know the specific side effects that sometimes result from taking medication and what to do when these problems occur
	Negotiating medication issues with health care providers	To practice ways of obtaining assistance when problems occur with medication

flection, warmth and concern, and empathic understanding. After the first 6 months, the group continued to meet an average of once per week through the 1-year follow-up period.

Modular skills training. Two modules from the UCLA Social and Independent Living Skills Program (15) with highly prescribed curricula for teaching medication and symptom self-management were used in the twice-weekly group skills training sessions during a 6-month period. Each module consisted of a clinician's manual, a patient's workbook, and a videotape that demonstrated the skills to be learned. The skill areas for the two modules are listed in table 2 and represent the main goals of the program.

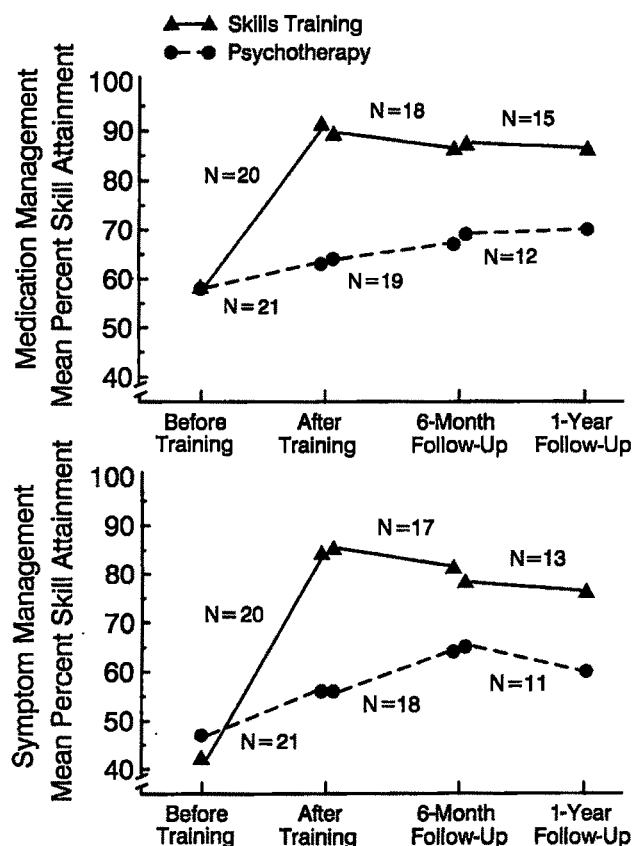
The modular procedures were designed to compensate for the cognitive and symptomatic interference with learning commonly found in schizophrenia. The patients proceeded through each skill area in a sequence of seven learning activities and exercises, starting with an introduction that highlighted the values and advantages of the training. The introduction used cognitive restructuring principles that, combined with the abundant positive social reinforcement delivered by the group leader throughout all learning activities, aimed to overcome the lack of motivation experienced by many schizophrenic patients. The next two learning activities—video modeling and behavioral rehearsal or role playing—were designed to engage the patients' attention and participation through the use of graphic demonstrations, maximal success experiences, and video feedback. Focused instructions, prompting, and coaching with immediate positive feedback were aimed at overcoming the obstacles to learning that arise from psychopathology and cognitive deficits.

The fourth and fifth learning activities were intended

to teach patients how to cope with frequently encountered obstacles to performing their newly acquired skills in their natural environments. The resource management activity was designed to teach patients how to gather the resources necessary for implementing a particular skill; for example, access to a telephone for making a clinic appointment and access to transportation were prerequisites for using the skills regarding negotiations about medication problems with their doctors or seeking early intervention to prevent a relapse. The outcome problem-solving activity taught patients how to respond when the environment failed to provide the expected and desired outcome after their performance of a particular skill. For example, if an individual got to the clinic to report a medication side effect or the emergence of warning signs of relapse, it was important to know how to handle the exigency of the doctor's having been called away on an emergency or being sick that day. Through repeated practice exercises, these two learning activities were intended to teach patients a general problem-solving strategy for illness self-management and to overcome the inadequacies in social problem solving and self-assertiveness so frequently noted in schizophrenic patients.

The final two learning activities—in vivo exercises and homework assignments—were used to facilitate the transfer of training to the patients' living environments. In each of these activities, the group leader helped the patients to fine-tune their performances, resulting in more independent action. Training sessions for both modules were scheduled twice weekly for 6 months, and each module took approximately 90 minutes per session. Training continued until all patients achieved the specified mastery criterion of 80% of the skills, as determined by role-playing tests. After the 6 months of

FIGURE 1. Attainment and Retention of Skills in Medication and Symptom Management by Schizophrenic Patients Receiving Skills Training or Group Psychotherapy^a



^aSignificant effect of training for patients receiving social skills training (medication management: $F=75.10$, $df=1, 34$, $p<0.0001$; symptom management: $F=36.23$, $df=1, 32$, $p<0.0001$). Significant difference between groups in medication management skills at 6 and 12 months ($F=56.45$, $df=1, 30$, $p<0.0001$, and $F=40.28$, $df=1, 25$, $p<0.0001$, respectively), and significant difference between groups in symptom management skills at 6 and 12 months ($F=6.34$, $df=1, 28$, $p<0.02$, and $F=9.41$, $df=1, 22$, $p<0.005$, respectively).

training in these two modules, the subjects in this condition continued to meet for the remainder of the 1-year follow-up period once a week in a basic social skills training group (5) aimed at individual goal setting and interpersonal problem solving.

Assessment Measures

All subjects were evaluated with the Brief Psychiatric Rating Scale (BPRS) and the Schedule for Assessment of Negative Symptoms (16) at baseline and at regular monthly intervals thereafter. The BPRS ratings were performed by experienced clinicians who had been trained until they reached an interrater reliability of 0.80 (intraclass r) or greater. Although attempts were made to keep the raters blind to the subjects' psychosocial treatment conditions, a few patients revealed this information during the rating sessions.

Skill attainment was assessed through the subjects' behavioral performances in a series of standardized role-playing tests. Seven scenes taken from the essential skill areas of the medication management and symptom management modules were administered, and the patients' performances were rated on a 4-point Likert-type scale ranging from "poor" to "excellent." Each point on the scale was defined operationally and included verbal content and nonverbal and paralinguistic skills relevant to each of the skills that were taught in the modules. Ratings of each scene were summed to yield a total score reflecting the acquisition of skills for each module. Role-playing tests have been shown to be valid means of assessing the social competence of patients with schizophrenia or major affective disorders (17).

The skill assessments (14) were made by research assistants who were initially trained to reliably rate the role-playing tests by practicing independently with clinic patients not participating in the study until each behavioral category was rated at or above 0.80; the standard rating by which the assistants were judged was made by the first author. Subsequently, interrater reliability was assessed and maintained through joint ratings of 15% of the tests in which the first author was the criterion rater. Interrater reliability remained high throughout the study, ranging between 0.82 and 1.00 (kappa coefficients).

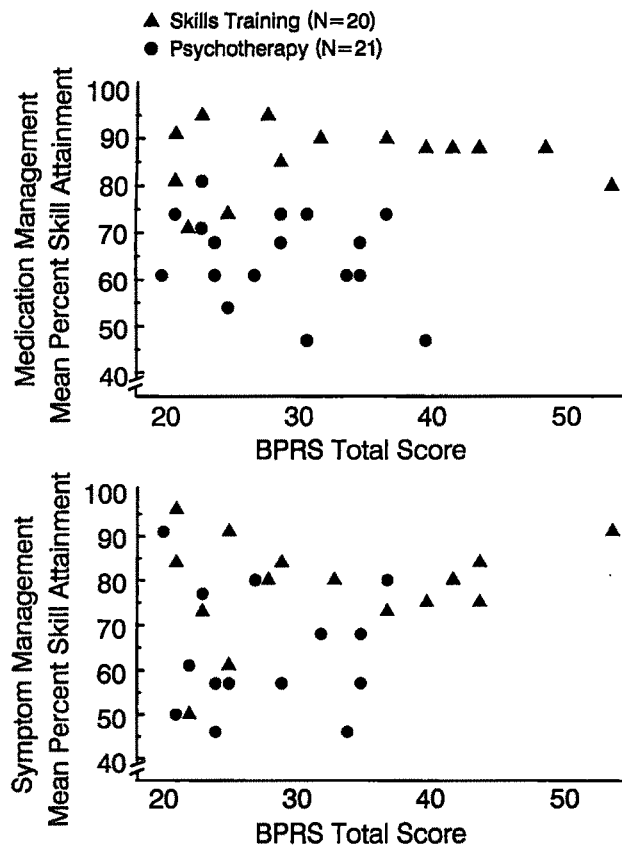
RESULTS

Because attrition occurred during the 12-month follow-up period, most but not all subjects were rated on the skill levels at each rating point. Over the full 18-month study period, more subjects in the skills training condition (15 of 20) than in the supportive group therapy (12 of 21) remained in the study; this difference almost reached statistical significance. The psychiatric and social histories, pretreatment BPRS scores, and pretreatment scores on the skills tests did not differentiate the subjects who dropped out from the subjects who completed the intensive treatment and full follow-ups.

Group by Trial analyses of variance were used to evaluate skills acquisition in the two psychosocial treatment conditions. As shown in figure 1, there was a significant effect of training in both modules for the subjects who received the social skills training but not for the subjects in group therapy. The pretreatment mean skill levels for the two psychosocial conditions were virtually identical, while the posttreatment means diverged considerably, indicating that the subjects who received modular skills training displayed a marked increase in knowledge and skill and the subjects in group therapy did not improve in these domains.

The durability of learning over time was evaluated by comparing the posttreatment means with the 6-month follow-up means and then comparing the 6-month follow-up means with the means at the 12-month follow-

FIGURE 2. Relationship Between Baseline BPRS Total Score and Subsequent Medication and Symptom Management Skills for Schizophrenic Patients Receiving Skills Training or Group Psychotherapy



up. As depicted in figure 1, for both modules there was little erosion of skill levels during the 12-month follow-up period. The 6-month follow-up means for the subjects in skills training paralleled their posttreatment means and were significantly different from the means of the subjects receiving group therapy. Of interest was the modest, albeit nonsignificant, increase in skills shown by the subjects in group therapy over the 1-year follow-up period.

Do Psychotic Symptoms Impede Learning of Skills?

Analyses were conducted to determine whether cognitive deficits, negative symptoms, and other measures of psychopathology interfered with the patients' acquisition of the knowledge and skills contained in the modules. In particular, we hypothesized that 1) patients rated high on conceptual disorganization and on the negative symptom subscales of the BPRS would show impaired learning in the two modules but that 2) subjects with mild to moderate levels of thought disorder and negative symptoms would learn well.

In the skills training condition, however, there was no relationship between the baseline levels of psychopathology and posttreatment knowledge and skill in medication and symptom management. As depicted in

TABLE 3. Correlations Between Baseline BPRS Scores and Posttreatment Skill Levels for 20 Schizophrenic Patients Receiving Skills Training

Baseline BPRS Measure	Correlation (r) With Posttreatment Skills	
	Medication Management	Symptom Management
Total score	-0.01	-0.40
Positive symptom scores	-0.05	-0.37
Hallucinations	-0.14	-0.24
Unusual thought content	-0.06	-0.51 ^a
Conceptual disorganization	0.14	-0.01
Negative symptom scores	-0.15	-0.21
Blunted affect	-0.29	-0.30
Emotional withdrawal	0.07	-0.17
Motor retardation	0.12	0.27
Median correlation	-0.06	-0.21

^ap=0.03 (df=18).

figure 2, the patients who received skills training performed well on the posttreatment assessments of knowledge and skills regardless of the initial level of psychopathology. Correlations between the initial BPRS ratings and posttreatment skill levels are presented in table 3 for the patients in the skills training condition. While the relationships between symptoms and skills acquired were in the expected negative direction in 14 of the 18 correlations, the one statistically significant correlation was well within what would be expected by chance. Nor were there any significant relationships between mean levels of psychopathology over the 18-month study period and the durability of skills. It should also be pointed out that the subjects in the skills training condition acquired substantial knowledge and skills from their participation in the modules even though they were somewhat more clinically ill at the start of treatment than their counterparts who received group therapy—their symptoms on the BPRS were higher but not statistically so.

The ability of the modular training to effectively overcome obstacles to learning posed by psychopathology and social disability was also seen in the lack of positive correlations between baseline and posttreatment skill and knowledge levels among the subjects in the skills training condition, as well as between baseline ratings of overall work and social functioning and amount of skills learned. The failure to find associations between the subjects' baseline amount and quality of social skills and functioning and their acquisition of knowledge and skills from the modules suggested that the skills training modules could override pretreatment levels of social adjustment in producing a learning effect.

Does Skills Training Displace Psychopathology?

Across the entire pool of subjects in both psychosocial treatment conditions, significant symptom improvements occurred from baseline to the point where pharmacotherapy had stabilized the subjects and they began their participation in either skills training or

group therapy. Symptomatic improvement continued through the 6-month follow-up period. The mean BPRS scores across the entire group were 36.2 (SD=10.6) at intake, 31.2 (SD=8.6) at the start of the psychosocial treatments, and 28.6 (SD=7.9) at the 6-month follow-up ($F=9.77$, $df=2, 35$, $p<0.0004$). Likewise, across the entire pool of subjects the mean score on the Schedule for Assessment of Negative Symptoms fell from 1.02 (SD=0.53) at the start of psychosocial treatment to 0.82 (SD=0.43) at the end of 6 months of psychosocial treatment ($F=6.31$, $df=1, 30$, $p<0.018$).

The subjects in both psychosocial treatment conditions improved substantially from baseline to the end of the period of intensive therapy. Although the subjects in the skills training condition improved somewhat more in terms of total BPRS symptoms, this difference in improvement rates was not significant ($F<1$, $df=1, 36$, *n.s.*) and could be attributed to the somewhat higher initial levels of psychopathology experienced by the subjects randomly assigned to the skills training condition. Similarly, the subjects in the skills training condition did not improve significantly more on negative symptoms than their counterparts receiving group therapy ($F<1$, $df=1, 29$, *n.s.*).

DISCUSSION

The use of structured learning and cognitive therapy in the design of modules to teach illness self-management skills appeared to be instrumental in achieving high levels of knowledge and skill in schizophrenic patients. The substantial and sustained learning of medication and symptom self-management skills by patients could not be simply ascribed to the patients' immersion in an active and educationally oriented outpatient clinic, as comparison patients receiving the same overall clinic treatment and group therapy in lieu of skills training did not show significant learning effects. It is of interest, however, that the frequent interactions with positive and engaging clinicians did have an educational impact on the comparison group patients, since their knowledge and skills showed a small but distinct upward trend over the 18 months of their participation in the study. The impressive learning effects found in this study cannot be secondary to symptom improvements since the patients in the group therapy condition showed significant symptomatic improvements without a corresponding acquisition of knowledge and skills.

The correlations between baseline ratings of psychopathology and subsequent skills performance were relatively small. The patients appeared to be able to learn substantially, regardless of initial psychopathology. It was encouraging that the modules, purposely designed to provide a special educational milieu for cognitively and symptomatically impaired schizophrenic patients, did appear to override these impairments and achieve their intended educational effects. These findings replicate and extend those reported by Mueser et al. (18), who found no relationship of symptoms to changes in

skills among 55 schizophrenic patients enrolled in social skills training.

The ability of the modules to compensate for the patients' cognitive and symptomatic impairments must be qualified by the nature of the subject group; that is, the participants in this study were selected and survived the training because they were relatively stable ambulatory patients with only moderate levels of psychopathology. For example, one subject who had extremely high negative symptoms at the start of treatment learned poorly. As veterans, the subjects in this study had higher premorbid levels of social adjustment than nonveteran schizophrenic subjects might be expected to have, and, thus, generalizations to more disabled populations of schizophrenic patients should be made cautiously. Another caveat came from the social skills trainers in this study, who reported that more arduous training efforts were required to impart knowledge and skills to the more symptomatic patients. For example, patients with higher levels of preoccupying delusions or thought disorder required substantially more repetition and between-session review to sustain their progress.

The learning effects were robust, resisting erosion over the 12-month follow-up period, during which time only a single "booster" session was required to maintain the patients' knowledge and skills at their post-training levels. Also reflecting the robustness of the learning effects of the modules were the lack of correlations between amount of knowledge and skills acquired and sociodemographic and baseline clinical variables, including duration of illness, number of previous hospitalizations, and premorbid social adjustment. This means that the training design was able to "mainstream" patients through the educational modules, much as our public school system often succeeds in mainstreaming normal and handicapped children from widely varied backgrounds in classrooms. Concerns that social skills training might be overstimulating or stressful for vulnerable schizophrenic patients were allayed by findings that scores on indexes of stress and tension, such as the BPRS subscales for anxiety, depression, and distractibility, actually diminished as training was delivered.

Despite the strengths of the present study (clear specification of the intervention, use of state-of-the-art measures for diagnosis and clinical assessment, generally blind and independent assessments, and use of a randomized comparison group that included a control for contact time), questions may be raised about the generalization of the skills and knowledge learned in the modules into patients' real-life circumstances. While formal testing is still being conducted to assess generalization over time and across settings, anecdotal reports by patients and people close to them revealed that nearly all of the patients systematically and regularly monitored their warning signs throughout the time that the modules were being taught—6 months. Many patients routinely brought their medication self-evaluation forms to appointments with their psychia-

trists for review. In one case, a patient taught his schizophrenic roommate how to monitor medication effects by using forms he had obtained during module training because the patient was disturbed by the roommate's erratic behavior, which the patient attributed to poor medication compliance.

A unique feature of the skills training modules used in this study was the video-mediated educational process, which for a wide variety of patient education purposes has been shown to consistently raise short-term knowledge, even among patients with poor literacy skills (19). Future extensions of this technology may be found in video disk, computer-assisted instruction that can reinforce learned constructs, provide immediate feedback, and promote cognitive rehearsal. These technological advancements can be programmed for interactive learning, individualized, and presented at times more convenient for the patient (20).

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Alprazolam Plasma Concentrations and Treatment Response in Panic Disorder and Agoraphobia

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Objective: The authors' goal was to evaluate the relationship between plasma concentrations of alprazolam and both treatment response and side effects in patients with panic disorder and agoraphobia. **Method:** Ninety-six patients with panic disorder and agoraphobia were treated at three sites in a 6-week, fixed-dose, double-blind, placebo-controlled, dose-response study of 2 mg/day or 6 mg/day of alprazolam. Assessments were made of panic attacks, avoidance behavior, generalized anxiety, and global response. Blood samples were collected throughout the study and analyzed for alprazolam and other benzodiazepines. **Results:** Patient compliance with the protocol was judged to be good on the basis of plasma concentrations. According to logistic regression analysis, the relationships between plasma alprazolam concentration and response, as reflected by number of panic attacks reported, phobia ratings, physicians' and patients' ratings of global improvement, and the emergence of side effects, were significant. However, there was no significant relationship between plasma alprazolam concentration and the degree of generalized anxiety symptoms. **Conclusions:** The authors conclude that plasma concentration of alprazolam is related to treatment response, particularly in panic attacks. The alprazolam concentration associated with treatment response or with emergence of a given side effect varied widely among individuals, highlighting the necessity for individualized dose adjustment to obtain optimal treatment response while minimizing side effects.

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Studies of the triazolobenzodiazepine alprazolam in the treatment of panic-related disorders have repeatedly demonstrated the efficacy of this compound, but they have indicated that a wide range of doses may be necessary for control of panic attacks (1-4). This wide range could be due to a number of factors that are not mutually exclusive, such as 1) pharmacokinetic variability, resulting in variable alprazolam plasma concentrations from a given dose, 2) differences in severity of the panic-related disorder, 3) intersubject vari-

ability in response to alprazolam, and 4) self-medication with other benzodiazepines.

Intersubject differences in alprazolam pharmacokinetics may be a major factor in the variability of effective dose, since administration of the same dose to homogeneous patient samples can result in a three- to four-fold variability in steady-state plasma alprazolam concentration (3, 5). Although the results of previous studies have demonstrated a relationship between alprazolam dose and plasma concentration (6, 7), the relationship between alprazolam plasma concentration and clinical outcome has not been clearly elucidated.

The present study was a three-site, placebo-controlled trial. It was undertaken to evaluate the relationships between alprazolam dose, plasma concentration, and treatment response in patients with panic disorder. A fixed-dose study design was used to evaluate a relatively low and a relatively high dose of the drug. This design may be more appropriate for evaluating relationships between concentration and treatment response (8) than the adjustable-dose design used in previous alprazolam efficacy studies. This report presents the analysis of the relationship between treatment response measures and plasma alprazolam levels in pa-

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tients with panic disorder who were receiving 2 mg/day of alprazolam, 6 mg/day of alprazolam, or placebo.

We also address the use of plasma benzodiazepine concentrations to assess protocol compliance. Efficacy and side effect results from the study have been reported elsewhere (9). A preliminary report on the logistic regression methodology also has been presented elsewhere (10), and the concentration data obtained from that study have been used to evaluate the feasibility of subjecting clinical efficacy trial data to population pharmacokinetic analyses (11).

METHOD

Patients and Study Design

The complete study design, including details of patient recruitment and screening and descriptions of the clinical evaluation scales and diagnostic criteria, has been described in a previous report (9). In brief, this was a double-blind, placebo-controlled, fixed-dose study evaluating placebo, 2 mg/day of alprazolam, and 6 mg/day of alprazolam. The subjects were 96 patients who met *DSM-III* criteria for panic disorder or agoraphobia with panic attacks after evaluation with the Structured Clinical Interview for *DSM-III*, Upjohn Version (12). Seventy percent of the subjects were women and 30% were men; their mean age was 37.1 years. From 77% to 90% in each treatment group met criteria for agoraphobia (the difference among the groups in the proportion of patients with agoraphobia was not significant). The protocol was approved by the institutional review board of each study site, and all subjects gave written informed consent before participating in the trial.

After diagnostic, medical, and laboratory examinations were completed, subjects were randomly assigned to three treatment groups: 30 were given 2 mg/day of alprazolam, 31 were given 6 mg/day of alprazolam, and 35 were given placebo. The groups were comparable in age; there were more male subjects in the group given 2 mg/day of alprazolam. A psychotropic drug washout period of at least 1 week preceded the baseline evaluation. Patients then received either placebo or 1 mg/day of alprazolam, with a dose escalation schedule ensuring that the target dose was achieved by day 3 for the patients given 2 mg/day and by day 18 for the patients given 6 mg/day. The trial lasted 6 weeks and was followed by a 3-week drug taper. Evaluations were performed at baseline and after 1, 2, 3, 4, and 6 weeks of treatment; 15 (45.5%) of the patients given placebo, 23 (76.7%) of the patients given 2 mg of alprazolam, and 16 (48.4%) of the patients given 6 mg of alprazolam completed the 6-week trial. The methods of dealing with this differential dropout rate are discussed later in this paper and elsewhere (9).

Blood samples were obtained from the subjects at each evaluation time. In addition to the times blood was drawn, the actual times the medication or placebo was administered on the day of sampling and the previous

TABLE 1. Criteria for Classification of Response to Alprazolam Treatment for Panic Disorder

Measure of Treatment Response	Response Classification		
	Major	Moderate	None
Reduction from baseline in total number of panic attacks (%)	>75	25–75	<25
Reduction from baseline in Hamilton anxiety score (%)	>50	25–50	<25
Overall phobia score	0–3 ^a	4–6 ^b	7–10 ^c
Change from baseline in main phobia fear and avoidance score (%)	>50	25–50	<25
Change from baseline in agoraphobia fear and avoidance score (%)	>50	25–50	<25
Physician-rated global improvement scale score	9–10 ^d	7–8 ^e	0–6 ^f
Patient-rated global improvement scale score	9–10 ^d	7–8 ^e	0–6 ^f

^aNot at all to mildly anxious.

^bModerately anxious.

^cMarkedly to extremely anxious.

^dMarkedly improved or back to normal.

^eModerately improved.

^fWorse to a little better.

day were recorded. To generate a random selection of collection times after the previous alprazolam dose, no time of blood sample collection was specified within the protocol. Ten-ml blood samples were collected in heparinized tubes and centrifuged, and the plasma was separated and frozen until analysis.

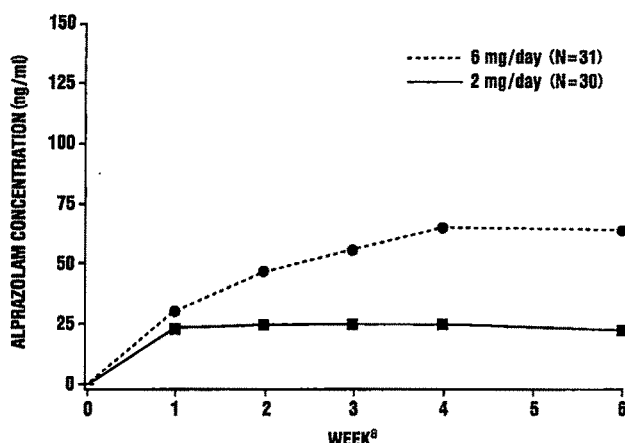
Benzodiazepine Assays

Plasma samples from all patients were analyzed for not only alprazolam but also diazepam and desmethyldiazepam to determine if patients were medicating themselves with other benzodiazepines (excluding lorazepam). Alprazolam, diazepam, and desmethyldiazepam concentrations were determined by gas-liquid chromatography with electron-capture detection by previously reported methods (13, 14).

Data Analysis

Treatment response measures. Treatment response was classified for each of the following efficacy measures: total number of major panic attacks per week, total score on the Hamilton Rating Scale for Anxiety (15) (used to measure overall anxiety, apart from specific panic attacks), overall phobia rating, fear and avoidance factors of the main phobia and agoraphobia ratings derived from the work of Marks and Mathews (16), physician-rated global improvement scale score, and patient-rated global improvement scale score. We defined categories of major, moderate, or no response for each measure, as shown in table 1.

Logistic regression analysis. The relationship between treatment response and plasma alprazolam concentrations was examined with logistic regression analysis (17, 18) of data from the three treatment groups. Patient response classification and plasma alprazolam

FIGURE 1. Mean Plasma Alprazolam Concentrations of Patients With Panic Disorder Given 2 mg/day or 6 mg/day

*Significant difference between groups at week 2 ($t=3.86$, $df=52$, $p=0.0003$), week 3 ($t=6.02$, $df=49$, $p=0.0001$), week 4 ($t=7.04$, $df=47$, $p=0.0001$), and week 6 ($t=6.63$, $df=37$, $p=0.0001$).

concentrations were fitted to a logistic response function with the CATMOD procedure of the Statistical Analysis System (19). Regression coefficient estimates generated from the fitting procedure then were used to calculate the probability of a patient's having a particular response (e.g., major, moderate, none) at a given alprazolam plasma concentration. The details of the analysis have been reported elsewhere (10).

RESULTS

Data for some of the 96 patients could not be included in some of the analyses due to the incompleteness of concentration and/or response data. The number of individuals for whom data were analyzed by each method is reported in each analytical section.

Compliance With Treatment

Only one patient in the placebo group had a positive alprazolam level at any evaluation time; this patient had a positive level at week 2. At baseline, six (20%) of the 30 placebo patients for whom this information was available had positive diazepam levels, and nine (30%) had positive desmethyldiazepam levels. The percent of placebo patients with positive levels for diazepam and/or desmethyldiazepam remained relatively constant throughout the study.

No patients given either 2 mg or 6 mg of alprazolam treatment for whom this information was available ($N=55$) had a positive alprazolam level at baseline. After therapy was initiated, positive alprazolam levels were detected in virtually all alprazolam-treated patients (96%–100% at different evaluation times). At baseline, nine (33%) of the available 27 patients given 2 mg/day of alprazolam and five (18%) of the available

28 patients given 6 mg/day of alprazolam had detectable diazepam and/or desmethyldiazepam concentrations. These percentages decreased during the study; at week 6 only two (8.7%) of 23 patients given 2 mg/day of alprazolam and one (6.2%) of 16 patients given 6 mg/day had detectable levels.

Mean Plasma Alprazolam Concentrations

Alprazolam plasma concentration data were available for 61 patients treated with alprazolam (30 of the patients given 2 mg/day and 31 of the patients given 6 mg/day). On average, each subject had four plasma level determinations. The majority of the samples were collected between 0 and 6 hours after medication administration. Mean plasma alprazolam concentrations for the two alprazolam treatment groups at each week of evaluation are shown in figure 1. Alprazolam concentrations differed significantly between the patients given 2 mg/day of alprazolam and those given 6 mg/day at weeks 2, 3, 4, and 6 (figure 1). At week 4, when all patients had been receiving their maximum alprazolam dose for at least 9 days, the mean alprazolam concentrations were 24.5 ng/ml ($SD=15.6$) for the patients given 2 mg/day and 65.2 ng/ml ($SD=24.4$) for the patients given 6 mg/day. Only 10% of the patients given 2 mg/day had plasma levels above 40 ng/ml, and none had a plasma level above 80 ng/ml. Conversely, approximately 80% of those given 6 mg/day had plasma levels above 40 ng/ml.

Response Relationship to Alprazolam Plasma Concentration

Data from the last evaluation period in the three treatment groups were analyzed by logistic regression. This is roughly equivalent to a week-6 endpoint-imputed analysis (i.e., the last observation was carried forward). The mean times of the last evaluations were 4.8 weeks ($SD=1.6$) for the placebo group, 5.1 weeks ($SD=1.2$) for the patients given 2 mg/day of alprazolam, and 4.8 weeks ($SD=1.4$) for the patients given 6 mg/day of alprazolam (there were more dropouts among the patients given placebo and those given 6 mg/day than among the patients given 2 mg/day). At these evaluation times, all patients were receiving their scheduled alprazolam dose except for three patients in the 6 mg/day group who had reached a dose of only 4 mg/day. These patients were included in the analysis because plasma concentration, not dose, was being evaluated as a predictor of response.

Number of Major Panic Attacks

At baseline, the mean number of panic attacks per week was 7.5 ($SD=9.9$) for the placebo group, 5.3 ($SD=4.9$) for the patients given 2 mg/day of alprazolam, and 6.6 ($SD=7.7$) for the patients given 6 mg/day of alprazolam. Among patients who completed the 6-week trial, the mean number of panic attacks per week

was 3.7 (SD=4.9) for the placebo group, 1.0 (SD=2.7) for the patients given 2 mg of alprazolam, and 1.0 (SD=2.8) for the patients given 6 mg of alprazolam. According to endpoint analysis, the mean number of panic attacks per week was 5.4 (SD=6.2) for the placebo group, 2.0 (SD=4.6) for the patients given 2 mg/day of alprazolam, and 1.9 (SD=3.9) for the patients given 6 mg/day of alprazolam. Both treatment groups improved more than the patients given placebo (9).

Plasma alprazolam concentration was a significant predictor of response assessed by the reduction of major panic attacks ($\chi^2=70.58$, $df=90$, $p=0.003$, likelihood ratio=0.935). A steady-state plasma alprazolam concentration of 15 ng/ml was necessary to achieve a 50% probability of being classified as a major responder, and a concentration of 48 ng/ml was necessary to achieve a 75% probability of being a major responder.

The calculated probability curves, based on the best-fit parameter estimates from the logistic regression model, and the actual response frequencies are presented in figure 2. The three individual graphs represent the predicted probabilities for responder classification over a range of drug concentrations for the three categories of response: major (greater than 75% reduction in panic attacks), moderate (25%–75% reduction), and none (less than 25% reduction). From these graphs, one can determine the probability of attaining the level of response associated with a particular alprazolam steady-state concentration by selecting the concentration and reading the numerical value associated with the curve at that concentration on the respective response graph of interest. At any given alprazolam concentration, the sum of the three probability values for the response classifications equals one.

Using the more stringent criterion for treatment response of having no panic attacks at the last visit, we found that 18 (67%) of 27 subjects with alprazolam concentrations greater than 40 ng/ml, eight (57%) of the 14 subjects with concentrations between 20–40 ng/ml, and eight (42%) of the 19 subjects with concentrations less than 20 ng/ml met this criterion.

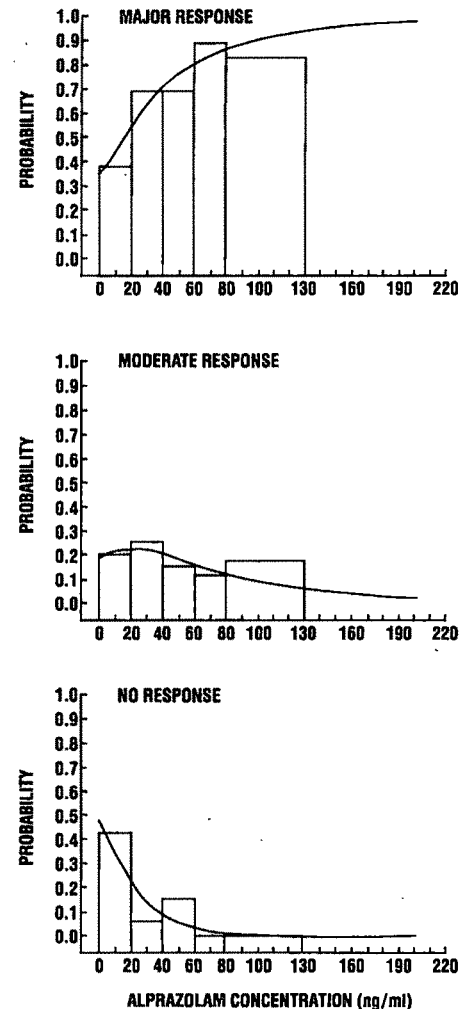
Hamilton Rating Scale for Anxiety

Logistic regression analysis showed no significant relationship between steady-state alprazolam plasma concentration and response classified on the basis of change in Hamilton anxiety score. According to this scale, approximately 70% of the patients were classified as either major or moderate responders at the lowest alprazolam concentrations.

Phobia Ratings

The five phobia ratings were 1) the overall phobia rating, 2) the main phobia fear score, 3) the main phobia avoidance score, 4) the agoraphobia fear score, and 5) the agoraphobia avoidance score. Alprazolam plasma concentration was a significant predictor for response based on the main phobia fear score ($\chi^2=76.24$,

FIGURE 2. Calculated Probability Curves and Observed Frequencies of Patients With Major, Moderate, or No Response to Alprazolam for Panic Disorder



$df=76$, $p=0.04$, likelihood ratio=0.471) and the agoraphobia fear score ($\chi^2=78.4$, $df=76$, $p=0.03$, likelihood ratio=0.403). However, the actual response frequencies on these scales varied considerably and inconsistently with increasing alprazolam concentrations. Therefore, the probability values should be interpreted cautiously. An alprazolam concentration of approximately 75 ng/ml was necessary to obtain a 50% probability of a patient's being classified as a major responder (greater than 50% reduction) by the main phobia fear score. The numbers of patients classified in each response group are presented in table 2. There were no significant relationships between response classification and plasma alprazolam concentration for the other three phobia ratings.

Physician-Rated and Patient-Rated Global Improvement Scales

There was a significant relationship between plasma alprazolam concentration and treatment response cate-

TABLE 2. Relation of Plasma Alprazolam Concentrations and Response Rates for Patients With Panic Disorder

Plasma Alprazolam Concentration	Response According to Main Phobia Fear Scale Score				Response According to Physician-Rated Global Improvement Scale				Response According to Patient-Rated Global Improvement Scale			
	N	Major	Moderate	None	N	Major	Moderate	None	N	Major	Moderate	None
0 ng/ml	26				29				29			
N		4	8	14		5	3	21		5	8	16
%		15	31	54		17	10	72		17	28	55
1-19 ng/ml	17				19				19			
N		4	3	10		3	9	7		5	8	6
%		24	18	59		16	47	37		26	42	32
20-39 ng/ml	11				14				14			
N		5	2	4		4	4	6		3	7	4
%		46	18	36		29	29	43		21	50	29
40-59 ng/ml	13				14				14			
N		5	3	5		6	5	3		7	4	3
%		39	23	39		43	36	21		50	29	21
60-79 ng/ml	7				7				7			
N		4	1	2		4	2	1		2	4	1
%		57	14	29		57	29	14		29	57	14
≥80 ng/ml	6				6				6			
N		3	0	3		0	5	1		3	2	1
%		50	0	50		0	83	17		50	33	17

gorized according to the physician-rated ($\chi^2=104.3$, $df=90$, $p=0.002$, likelihood ratio=0.143) and patient-rated ($\chi^2=94.46$, $df=90$, $p=0.02$, likelihood ratio=0.353) global improvement scales. Again, actual response frequencies did not consistently increase with increasing alprazolam concentrations. According to the calculated curve, the steady-state alprazolam plasma concentration necessary to result in a 50% probability of a patient being classified as a major responder (markedly improved or back to normal) on the physician-rated global improvement scale was 63 ng/ml. However, this finding should be interpreted cautiously because the actual frequencies of a major response on the physician-rated global scale rating varied widely as shown in table 2. The corresponding levels of response at the same concentration levels for the patient-rated global scale also are shown in table 2.

Treatment-Emergent Side Effects and Symptoms

Treatment-emergent symptoms and side effects were defined as those having a greater severity at the time of evaluation than at baseline. Seven of 42 symptoms were reported more frequently by patients given either 2 mg/day or 6 mg/day of alprazolam: sedation/drowsiness, ataxia/impaired coordination, slurred speech, nasal congestion, constipation, diarrhea, and decreased libido (9). Of these, more patients given 6 mg/day than patients given 2 mg/day reported ataxia/impaired coordination and slurred speech; similar numbers reported the remaining symptoms. Five of 42 symptoms (impaired mentation, insomnia, tachycardia/palpitations, tremor, and excessive sweating) were reported more frequently by patients given placebo (9).

The relationships between alprazolam concentration and the emergence of seven significantly and positively related symptoms and side effects were examined by logistic regression analysis of the data from week 4 and

the last evaluation visit. Similar results were obtained for both evaluations (table 3). At week 4, in addition to the symptoms and side effects listed in table 3, the emergence of tachycardia, a symptom of panic disorder, was significantly related to alprazolam concentrations; however, the probability of its emergence was greatest at low alprazolam concentrations.

DISCUSSION

Patient compliance with the protocol was judged to be good. The majority of patients took the study medications and refrained from medicating themselves with other benzodiazepine agents, and this was confirmed by obtaining plasma drug concentrations (although we did not measure concentration of lorazepam). This finding is essential to the further analyses of correlations between alprazolam concentration and response.

The doses in this study were selected on the basis of preliminary data indicating that doses of 2 mg/day and 6 mg/day of alprazolam should result in a wide range of steady-state plasma alprazolam concentrations and that more patients given 6 mg/day would respond to therapy (3, 4). The expected range and overlap of plasma alprazolam concentrations were achieved, and the two doses resulted in significantly different mean alprazolam concentrations. Thus, the selected doses resulted in data suitable for logistic regression analyses.

The results of our study demonstrate that patient response measured according to multiple dimensions is significantly related to steady-state plasma alprazolam concentrations. For panic attacks, the probability of a subject being classified as having a major, moderate, or no response was significantly and positively related to steady-state plasma alprazolam concentration. In a previous report (11), a pharmacokinetic analysis of the data obtained from the same patients showed that the

elimination of alprazolam in the patients who had major or moderate responses was approximately 40% less than that in the patients demonstrating no response. Reduced elimination of alprazolam resulted in higher steady-state plasma alprazolam concentrations for a given dose in patients classified as responders. This finding further supports a relationship between concentration and response.

Previous work indicates that there is an approximate relationship of 1 mg/day alprazolam dose to 10 ng/ml alprazolam steady-state concentration (7); our findings agree with this ratio. Therefore, the practitioner could then use our finding of a relationship between response and plasma concentration, based on logistic regression analysis, as a guide to total daily dose. For example, for panic attacks, a 75% probability of having a major response occurred at 48 ng/ml, roughly translating to a dose of 4–5 mg/day of alprazolam (given the caveats about intersubject variability). At approximately 1–2 mg/day alprazolam, there was a 50% probability of a major response for panic attacks. Ciraulo et al. (7) reported that, on global measures of impairment, significant improvement in subjects with panic disorder was achieved at plasma concentrations of 20 ng/ml and maximum response occurred at concentrations of 60 ng/ml and higher. However, Ciraulo et al. did not report information regarding response of specific symptoms. In our study, according to physician-rated and patient-rated global improvement scales, 53% of the subjects achieved a moderate response at 20 ng/ml and 80% at 60 ng/ml, which is similar to the data of Ciraulo et al. (7).

Plasma alprazolam concentration in our patients was not a significant predictor of treatment response based on Hamilton anxiety scores, probably due to the fact that the majority of patients with low alprazolam concentrations were classified as major responders on this outcome measure. In fact, only about 10% of patients with alprazolam concentrations between 20 ng/ml and 80 ng/ml were nonresponders on the Hamilton Rating Scale for Anxiety. Clinically, this means that most of the improvement in Hamilton anxiety scores (indicating more generalized or intercurrent anxiety symptoms) in these patients occurred at low doses and low plasma concentrations of alprazolam.

These results suggest that significant improvement in panic attacks occurs at higher alprazolam concentrations than those required for improvement in concomitant anxiety. Although there was clearly a reduction in panic attacks at lower alprazolam concentrations, higher concentrations increased the likelihood of being panic-free at the end of the trial. This is consistent with our previous finding that, although there were no significant differences in reduction of total panic attacks per week between the patients given 2 mg/day and those given 6 mg/day, there were significantly more patients who were panic-free among the patients given 6 mg/day (9).

Still higher concentrations of alprazolam were necessary to achieve a significant reduction in phobias. For the agoraphobia and main phobia fear scores, concen-

TABLE 3. Alprazolam Concentrations Associated With 50% Probability of Side Effects^a

Side Effect	Alprazolam Concentration (ng/ml) Associated With 50% Probability of Emergence	
	Week 4	Last Evaluation Period
Sedation	40	45
Ataxia	70	70
Memory problems	95	90
Slurred speech	100	90
Fatigue	120	110
Decreased libido	120	110
Sexual dysfunction	180	160

^aThe correlation between alprazolam concentration and emergence of side effects was positive for all side effects.

trations over 70 ng/ml were required to have a 50% probability of a major response. Response of the overall phobia score was not significantly related to alprazolam concentrations. It is difficult to explain these findings. They may be related to the fact that only a small number of patients were in the higher alprazolam concentration ranges and the fact that the actual response frequencies varied inconsistently with increasing alprazolam concentrations. Another explanation might be that phobias are not as responsive to alprazolam as are panic attacks and symptoms of anxiety. It also may be that phobias respond best when panic attacks are under the tightest control, i.e., at the higher plasma concentrations. In any case, this finding might explain why the phobias of some patients do not respond to medication, so that the addition of behavioral psychotherapy is indicated.

Alternatively, the phobias may respond, but only at higher alprazolam concentrations, or it might take longer than 6 weeks of drug treatment for phobias to respond. This possibility is consistent with the results using imipramine reported by Mavissakalian et al. (20). In a fixed-dose study, they observed that although panic attacks responded to lower doses and plasma concentrations of imipramine, higher doses and higher concentrations of imipramine were necessary for a good response in terms of reductions in phobic avoidance behavior.

The treatment-emergent symptoms and side effects we observed were those expected from administration of a benzodiazepine. According to logistic regression analysis, they were positively related to steady-state plasma alprazolam concentrations. The only treatment-emergent symptom or side effect that showed a negative correlation with alprazolam plasma concentration was tachycardia. Since tachycardia is a symptom of panic disorder, we would expect it to be better controlled at higher plasma alprazolam concentrations.

A comparison of the steady-state alprazolam concentrations necessary for a 50% probability of response and the 50% probability of the appearance of treatment-emergent side effects can be used to assess the benefit versus side effect ratio. A major response, defined by a reduction in the number of panic attacks, occurred at lower concentrations than those at which

the treatment-emergent symptom of sedation appeared (concentrations for 50% probability were 15 ng/ml for panic response versus 40 ng/ml for sedation). Other CNS side effects were not evident until much higher plasma alprazolam concentrations were obtained, e.g., ataxia at 70 ng/ml and slurred speech at 100 ng/ml. These results must be interpreted in the context of the study, because they are dependent on the rating scales used and the criteria for response classification. They also do not take into account very early treatment-emergent symptoms that may have developed within a few days but subsided as the patient became tolerant to the side effect or the fact that more patients dropped out of the higher alprazolam dose group.

The results of these analyses must not be interpreted as establishing a minimum effective alprazolam concentration or window of effective concentrations for the treatment of panic disorder. Rather, they should be interpreted as demonstrating that there is considerable between-patient variability in alprazolam pharmacokinetics, which explains some, but not all, of the variability in patient response at a given dose. They also offer an understanding that there exist different alprazolam concentrations (and, by inference, doses) which may be necessary to achieve improvement in specific symptoms of the panic syndrome. These findings further support the necessity for careful, individualized alprazolam dose adjustments to achieve the desired treatment response while minimizing undesirable side effects.

A final note of caution: we are not recommending the routine use of benzodiazepine plasma levels for clinical practice. Plasma level determinations of benzodiazepines have not been well standardized and are not readily available in many clinical laboratories. We believe that the use of benzodiazepine plasma levels requires further study in research settings before they can be considered for general practice.

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Panic Disorder History in the Families of Patients With Angiographically Normal Coronary Arteries

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Objective: The authors evaluated the diagnostic validity of an interview-based panic disorder diagnosis in cardiology chest pain patients with angiographically normal coronary arteries. **Method:** Patient probands with normal coronary arteries (N=65) were first contacted immediately after their normal angiogram and were given a structured diagnostic interview. On the basis of the results of the interview, probands were grouped as having panic disorder (N=19), panic attacks that did not meet frequency criteria for panic disorder (N=17), or no panic (N=29). At a later time, patient probands were recontacted and given a structured family-history interview that inquired about psychopathology in their first-degree biological relatives (N=544). **Results:** As predicted, panic disorder was significantly more prevalent among the first-degree relatives of probands with normal coronary arteries diagnosed with panic disorder or panic attacks than among the family members of probands with normal coronary arteries without panic (17.4% versus 15.7% versus 4.0%). Family members of probands with panic attacks were significantly more likely to be diagnosed with major depression than were the family members of probands with no panic; however, differences did not reach significance for family members of the panic disorder proband group. Groups did not differ significantly in familial alcoholism. **Conclusions:** These data support the construct validity of an interview-based panic disorder diagnosis among patients with chest pain and normal coronary arteries and suggest that these patients could benefit from treatment for panic disorder. (Am J Psychiatry 1992; 149:1563-1567)

Approximately one-third to one-half of cardiology patients with chest pain and normal coronary arteries meet diagnostic criteria for panic disorder (1, 2); however, several factors call into question the validity of an interview-based panic disorder diagnosis for these patients. Some researchers, for example, have maintained that the chest pain of patients with normal coronary arteries may best be explained by difficult to document cardiovascular abnormalities such as "microvascular angina" (3) or gastrointestinal abnormalities (4). Similarly, although some patients with normal coronary arteries technically meet the criteria for panic disorder, they demonstrate a demographic and symptom profile that is atypical for this diagnosis (5). These findings have led some researchers to suggest that the problems of patients with normal coronary arteries only mirror panic states (6). Thus, although many pa-

tients with normal coronary arteries do meet the criteria for an interview-based panic disorder diagnosis, additional corroborating evidence would appear to be necessary to support the validity of this diagnosis in patients with normal coronary arteries.

Assessment of familial patterns of mental disorder is commonly used to evaluate the validity of putative diagnostic entities (7). It is well documented that the risk for panic disorder in the first-degree relatives of psychiatric patients with panic disorder is two to five times higher than that in control samples (8, 9). Similarly, studies show that 56%–67% of panic disorder patients have at least one first-degree relative with panic disorder (8, 9); again, this is a much higher rate than that found in the general population.

If, as we maintain, panic disorder is a valid diagnosis in patients with chest pain and normal coronary arteries, we would predict a high risk for panic disorder in the first-degree relatives of patients who had normal coronary arteries and this diagnosis, but not in the relatives of other patients with normal coronary arteries. Furthermore, we would expect familial risk for panic disorder among patient probands with normal coronary arteries and a diagnosis of panic disorder to be compa-

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rable to that among probands with panic disorder identified in psychiatric samples (i.e., 15%–20%) (8, 9). For cardiology patients with normal coronary arteries who did not have a diagnosis of panic disorder, however, we would expect a familial rate of panic disorder that is comparable to that found in normal control subjects (3%–5%). Secondly, because major depression and alcoholism commonly co-occur with panic disorder (8, 10, 11), we would also expect to find higher rates of these disorders in the relatives of patients with normal coronary arteries and with panic disorder than in the relatives of other patients with normal coronary arteries. The purpose of this study was to test these predictions.

METHOD

Subjects

For this study we attempted to recontact all 94 patients with normal coronary arteries and chest pain who were originally assessed by Beitman et al. (1) approximately 3 years before the present study period. At that time, patients were recruited through a university cardiology clinic immediately after cardiac catheterization. To participate in the original study, patients had to have less than 30% stenosis of all major epicardial arteries and no other cardiac abnormalities that could explain their chest pain. The 65 patients we were able to contact at the follow-up assessment served as proband informants for this study. The final proband group consisted of 20 women and 45 men with a mean age of 56.1 years (SD=11.2 years). Comparisons between participants (N=65) and nonparticipants (N=29), using the original baseline data obtained by Beitman et al. (1), revealed no significant differences on diagnostic variables related to the current study.

Procedure

On the original contact (baseline), Beitman et al. (1) administered the Structured Clinical Interview for DSM-III (SCID) (12) to each patient. On recontact, approximately 3 years later (follow-up), we administered the Family Informant Schedule and Criteria adapted for DSM-III-R (13) to patient probands in order to assess panic disorder, major depression, and alcoholism in all biological, adult, first-degree relatives aged 18 or older, living or deceased, for whom there was adequate information (N=544). The Family Informant Schedule and Criteria is an extension of the Family History Research Diagnostic Criteria developed by Endicott et al. (14). The interview is designed to allow a clinician interviewer to systematically obtain diagnostic information on family members from a proband informant. Rules for coding diagnostic certainty include three categories: definite, probable, and possible. We assigned diagnoses to family members only if they were coded with a definite level of diagnostic certainty.

Using a graded set of techniques for locating study sub-

jects for follow-up, outlined by Russell Noyes (personal communication, March 1989), we attempted to recontact all 94 patients assessed by Beitman et al. (1) during the baseline phase. Sixty-five patients (69%) gave informed consent and served as proband informants. Of the remaining 29 patients, we were unable to locate 19, nine refused to participate, and one was deceased.

On telephone contact, we attempted to set up an appointment for patients to come to our clinic (N=21) to be interviewed; if this was not possible, we attempted to arrange to interview the patient over the telephone (N=44). The interviewer (M.G.K.) was blind to patients' baseline diagnoses. Patients were paid for their participation.

Study Groups and Dependent Variables

For all study analyses, the probands and their first-degree relatives were grouped on the basis of proband baseline SCID diagnosis. Three groups were formed: panic disorder probands, who met all DSM-III criteria for panic disorder; panic attack probands, who experienced panic attacks but not at the frequency required for a diagnosis of panic disorder; and probands with no panic, who did not experience panic attacks. There were two dependent variables of interest in this study: the percentage of first-degree relatives of probands with a study diagnosis (panic disorder, major depression, alcoholism) and the percentage of probands with at least one first-degree relative with a study diagnosis.

RESULTS

Table 1 shows sample characteristics of probands and their first-degree relatives for the three proband groups. Statistical comparisons were accomplished by using analysis of variance for continuously distributed variables and chi-square tests of association for dichotomous variables. The only significant group difference for these variables was the age of study probands. As shown, the probands with panic disorder were significantly younger than probands with no panic; the age of probands with panic attacks was intermediate and not significantly different from the other two proband groups (Tukey's multiple comparison test, $\alpha=0.05$).

Group comparisons on the percentage of probands' first-degree relatives with panic disorder confirmed study predictions. The overall 2 (familial panic disorder diagnosed versus not diagnosed) \times 3 (panic attack versus panic disorder versus no panic disorder proband group membership) chi-square analysis was significant ($\chi^2=18.58$, $df=2$, $N=544$, $p<0.01$). As shown in figure 1, the panic disorder and panic attack proband relative groups did not differ significantly in the percent of members diagnosed with panic disorder (17.4%, $N=29$ of 167 relatives, versus 15.7%, $N=22$ of 140 relatives, respectively). However, both of these relative groups had significantly more members diagnosed with panic disorder than was true for the group made up of the

TABLE 1. Characteristics of Probands With Chest Pain and Normal Coronary Arteries and of First-Degree Relatives, by Proband's Panic Attack Status

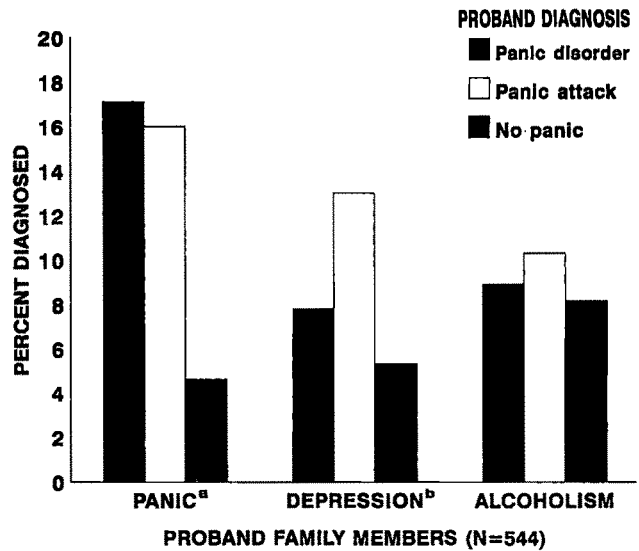
Group and Item	Proband Group		
	Panic Disorder	Panic Attack	No Panic
Probands			
Number	19	17	29
Gender			
Male			
Number	14	12	19
Percent	73.7	70.6	65.5
Female			
Number	5	5	10
Percent	26.3	29.4	34.5
Age (years) ^a			
Mean	51.2	54.7	60.2
SD	11.3	10.6	11.4
First-degree relatives			
Number	167	140	237
Members per family			
Mean	8.8	8.2	8.2
SD	4.3	3.7	3.4
Gender			
Male			
Number	86	71	123
Percent	51.5	50.7	51.9
Female			
Number	81	69	114
Percent	48.5	49.3	48.1
Age (years)			
Mean	49.5	50.5	54.3
SD	7.4	10.7	8.7

^aSignificant group difference ($F=3.93$, $df=2$, 64 , $p<0.05$).

relatives of the no panic disorder probands (4.0%, $N=11$ of 237 relatives).

Figure 1 also shows proband group differences in the percentage of first-degree relatives diagnosed with major depression. As predicted, the chi-square test confirmed that there was a significant overall effect for group membership ($\chi^2=6.67$, $df=2$, $N=544$, $p<0.05$). Again, as predicted, follow-up tests showed that probands with panic attacks had a higher percentage of first-degree relatives with major depression than did probands with no panic (12.9%, $N=18$, versus 5.5%, $N=13$; figure 1). However, failing to confirm study predictions, probands with panic disorder did not differ significantly from either of the other two proband groups on this variable. Finally, and again failing to confirm study predictions, proband groups were highly similar in the extent to which alcoholism was diagnosed for first-degree relatives (figure 1).

Table 2 shows proband group comparisons of the percentage of probands having at least one first-degree relative with panic disorder, major depression, and alcoholism. As shown, the overall group comparisons for panic disorder were significant. Compared to probands with no panic, significantly more probands with panic disorder and probands with panic attacks had at least one first-degree relative with panic disorder ($\chi^2=8.53$, $df=1$, $N=48$, $p<0.01$; $\chi^2=4.60$, $df=1$, $N=46$, $p<0.05$, respectively). Again, the panic attack and panic disorder

FIGURE 1. DSM-III Diagnoses in First-Degree Relatives of Probands With Chest Pain and Normal Coronary Arteries, by Proband's Panic Attack Status

^aSignificant difference between family members in the panic disorder proband group and those in the no panic proband group ($\chi^2=15.72$, $df=1$, $N=404$, $p<0.01$) and between family members in the panic attack proband group and those in the no panic proband group ($\chi^2=10.70$, $df=1$, $N=377$, $p<0.01$).

^bSignificant difference between family members in the panic attack proband group and those in the no panic proband group ($\chi^2=6.47$, $df=1$, $N=377$, $p<0.01$).

proband groups did not differ significantly on this variable. Thus, the pattern of group differences in the percentage of probands with any panic disordered relatives confirms study predictions and parallels group comparisons of the total percentage of family members diagnosed with panic disorder reported earlier.

Table 2 also shows that, compared to the no panic group, the panic attack group, but not the panic disorder group, had a higher percentage of probands with at least one relative diagnosed with major depression. Table 2 shows that the overall test of this effect approached statistical significance. Exploring the source of this statistical trend further, we again found that only differences between the panic attack and the no panic proband groups were significant ($\chi^2=4.50$, $df=1$, $N=46$, $p<0.05$). Thus, study predictions for this variable were confirmed for the panic attack group but not for the panic disorder proband group. Finally, and again consistent with the negative findings for alcoholism noted earlier, table 2 shows that we found virtually no group difference in the percentage of probands with at least one first-degree relative diagnosed with alcoholism.

DISCUSSION

Study findings support the validity of an interview-based panic disorder diagnosis among patients with

TABLE 2. Probands With Chest Pain and Normal Coronary Arteries Who Had Relatives With DSM-III Diagnoses, by Proband's Panic Attack Status

Relative's DSM-III Diagnosis	Proband Group					
	Panic Disorder (N=19)		Panic Attack (N=17)		No Panic (N=29)	
	N	%	N	%	N	%
Panic disorder ^a	12	63.2	9	52.9	6	20.7
Major Depression ^b	6	31.6	10	58.8	8	27.6
Alcoholism	8	42.1	7	41.2	12	41.4

^aSignificant group effect ($\chi^2=9.76$, $df=2$, $N=65$, $p<0.01$).

^bNearly significant effect ($\chi^2=4.82$, $df=2$, $N=65$, $p<0.10$).

normal coronary arteries. As predicted, the percentage of first-degree relatives diagnosed with panic disorder was significantly higher for probands who themselves received an interview-based diagnosis of panic disorder (17.4%) or panic attack (15.7%) than for the relatives of probands not diagnosed with panic (4.0%). Similarly, we found that 63.2% of the probands with panic disorder and 52.9% of the probands with panic attacks had at least one first-degree relative with a panic disorder diagnosis; however, this was true for only 20.7% of the probands with no panic.

As predicted, these group differences correspond with past studies that compared familial psychopathology in psychiatric samples of panic disorder probands with that of normal control subjects (8, 9). This outcome would not have been expected, however, if panic symptoms in patients with normal coronary arteries only mirrored panic states, as has been suggested by some writers (3, 4, 6). Specifically, we were able to make largely accurate *a priori* predictions both about the direction and magnitude of group differences in familial panic disorder. If a condition other than panic disorder were actually the source of symptoms in patients with panic disorder and patients with panic attacks, there would be no reason to expect the specific group differences that we predicted and found. Therefore, the conclusion that panic disorder identified in patients with normal coronary arteries and their families is the same syndromal entity as panic disorder identified in psychiatric samples would appear to be the most parsimonious interpretation of these findings.

Findings associated with major depression and alcoholism, however, were somewhat less straightforward. Although these findings were partially supportive of study predictions, it is unclear why the family members of probands with panic attacks, but not of probands with panic disorder, showed higher levels of major depression than relatives of probands with no panic. Our failure to find group differences in familial rates of alcoholism may reflect earlier findings suggesting that alcohol-related problems are uncommon among patients with normal coronary arteries and panic disorder (1). In addition, at least one family study reports that while risk for alcoholism is higher among the family members

of agoraphobic patients with panic attacks, this is not the case for the relatives of probands with uncomplicated panic disorder (15). These findings may have implications for those of the present study, as Beitman et al. (1) reported very low levels of agoraphobic avoidance among the patients with panic and normal coronary arteries who were used as subjects in this study.

Several methodological features may limit the generalizability of these findings. First, there can be little question that our use of proband informants to gain diagnostic information about family members (family history method) will yield generally less accurate results than would have the direct interviewing of the family members themselves (family study method). For example, several studies that directly compared these two methods report that the family history method significantly underreports familial psychopathology (16, 17). On the basis of these findings, we could expect that the degree of familial psychopathology in all of our study groups was actually higher than that reported here. Nevertheless, because there is no reason to believe that such a bias should operate differentially among the proband groups, our study conclusions would appear to remain unaffected.

A second issue that may be relevant to the generalizability of these findings is the relative reliability of the telephone interview (68% of the study cohort) versus the personal interview (32% of the cohort) method used in data collection. Although few studies have directly compared these two methods, Colombotos (18) reported that both yielded similar results in a systematic question-and-answer format unrelated to psychiatry. More recently, Paulsen et al. (19) found that diagnoses of panic disorder, depression, and alcohol abuse (the same diagnoses assessed in the current study) could reliably be obtained by using a telephone interview. Using a 12- to 19-month test-retest design, Paulsen et al. reported kappa values ranging from 0.69 to 0.84. Because these values are comparable to, or greater than, those obtained for these diagnoses by using personal interviews (20), it would appear to be likely that the reliability of our data collection methods was adequate.

In addition to the previous interpretational caveats, there could have been an undetected interaction between proband informant diagnosis and response bias to family interview questions. For example, probands who experience panic attacks themselves could be more sensitized to panic symptoms in their relatives and hence more likely to report such symptoms. However, this interpretation appears to be inconsistent with past findings, noted earlier, which show that the family history method tends to underreport rather than overreport familial psychopathology. Beyond this observation, however, it is clear that the appropriate way of ruling out this potential interpretational confound is a replication of this study in which family members are interviewed directly.

Finally, although we do document hypothesized differences in the familial rate of panic disorder for probands with normal coronary arteries who themselves

either do or do not experience panic attacks, this study was not designed to assess the causes of these group differences. That is, although we argue that the pattern of study findings supports the validity of the panic disorder diagnosis among patients with normal coronary arteries, addressing the nature of the mechanisms by which panic disorder is transmitted to family members is well beyond the scope of this study. For example, because panic has been shown to have a genetic component (21), it may have been that the panic attack and panic disorder groups (but not the no panic group) were likely to share a panic-related genetic vulnerability with their biological family members. Alternatively, environmental factors affecting the likelihood of a diagnosis of panic may have been more common in the panic attack and panic disorder groups. Almost assuredly, some combination of these two explanations is more appropriate than is either alone.

In conclusion, these findings corroborate an increasing body of research showing that chest pain for which no medical cause can be firmly identified may be associated with panic disorder (22). Past studies have documented that the symptoms of many cardiology patients with undiagnosed chest pain meet descriptive diagnostic criteria for panic disorder (1, 2). Supporting the view that these are bona fide cases, the current study shows that panic disorder is common in the families of patients with panic and normal coronary arteries but not in the families of other patients with normal coronary arteries. Because effective treatments for panic disorder are available (8), it will be important that patients with normal coronary arteries are routinely evaluated for panic disorder and, when appropriate, referred for treatment.

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Phenomenology and Course of Psychiatric Disorders Associated With Combat-Related Posttraumatic Stress Disorder

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***Objective:** Studies indicate that chronic combat-related posttraumatic stress disorder (PTSD) is frequently associated with other psychiatric disorders. Questions regarding the nature and interrelationships of these conditions require clarification. The purpose of this study was to address primary and secondary illness relationships by focusing on the specific phenomenology and course of illness onset of PTSD comorbidity. **Method:** In order to minimize confounding factors, only outpatients without recent substance use disorders were included. Sixty subjects who had been exposed to severe combat stress, including veterans of Vietnam and veterans of World War II or Korea, 15 of whom were former prisoners of war, received structured assessments over serial evaluations. **Results:** PTSD was the most prevalent lifetime disorder followed by major depression, panic disorder, generalized anxiety disorder, and phobic disorder or symptoms. Endogenous-appearing features overlapping other clinical populations were common; however, some specific symptom patterns also were suggestive of traumatic influence. Unlike generalized anxiety disorder and past substance use, the mean onset of phobias, major depression, and panic disorder, respectively, occurred later than PTSD. **Conclusions:** These observations suggest that persistent conditions related to PTSD progress toward symptoms that are increasingly autonomous in their pattern of occurrence.*

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Among anxiety disorders in *DSM-III-R*, posttraumatic stress disorder (PTSD) is uniquely defined as being linked to external events, specifically, stressors that are overwhelming and extreme. As a syndrome PTSD is defined by symptoms denoting the reexperiencing of trauma, withdrawal, and numbing of responsiveness, and heightened arousal. PTSD has been found to be frequent in veterans of military combat (1, 2) and represents an important concern in providing care to the veteran population. Observations of the frequent occurrence of PTSD with other psychiatric disorders in combat veteran patients, however, challenge the specificity of the relationship of PTSD to overwhelming stress.

There are references in the more traditional psychiatric literature to anxiety and mood-related syndromes

other than PTSD per se as outcomes of trauma (3). One of the first studies to report the association of PTSD with psychiatric comorbidity and to use modern diagnostic categories was by Sierles et al. (4). In that study structured diagnostic assessments were administered to 26 hospitalized veterans, 24 of whom had served in combat in Vietnam. All but one (96%) of the patients met criteria for PTSD, 84% also met criteria for alcoholism or drug dependence, and several patients were noted to have antisocial personality, somatization disorder, and endogenous depression. Seventy-two percent and 64% of the patients were reported to have had past episodes of depression and severe anxiety, respectively. More recently, Davidson et al. (5) reported lifetime diagnoses also assessed by structured interviews of veterans of Vietnam or World War II combat who participated in a medication treatment study of PTSD. Fifty-nine percent of the 44 patients, all diagnosed with PTSD, also met lifetime criteria for major depression, 59% for alcoholism, 47% for generalized anxiety disorder, and 30% for panic disorder. Davidson et al. also reported that alcoholism, PTSD, generalized anxiety, panic, and depression represented, on average, the sequence of illness onset.

While these and other studies have been consistent

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with regard to PTSD comorbidity in clinical combat veteran populations, it has been important to confirm the association of PTSD and other psychiatric morbidity with epidemiologic investigations. As part of the Epidemiologic Catchment Area study, Helzer et al. (6) identified 25 cases of PTSD, some of which were combat-related, from a community sample. PTSD was associated with a twofold risk of other psychiatric disorders, with greatest risk being for obsessive-compulsive disorder, dysthymia, and manic-depression. The Vietnam Experience Study of the Centers for Disease Control (2) reported a 66% lifetime prevalence of anxiety or depression and a 39% prevalence of alcohol abuse or dependence among the 15% of war zone veterans found to have PTSD. The more recent National Vietnam Veterans Readjustment Study (1) included 406 male and 170 female veterans who were exposed to high war zone stress in Vietnam. These subjects and other military and civilian control subjects received direct diagnostic interviews and supplemental assessments. From this database Jordan et al. (7) reported a greater prevalence of alcoholism, dysthymia, major depression, obsessive-compulsive disorder, and antisocial personality in the group exposed to high war zone stress. All of these epidemiologic studies relied on the Diagnostic Interview Schedule, a highly structured instrument used by trained lay interviewers, to determine the presence of psychiatric disorders other than PTSD.

Thus, the observation that combat-related PTSD, particularly of a chronic nature, is frequently associated with other psychiatric morbidity is well documented from both clinical and epidemiologic data. There are, however, a number of important questions regarding the nature of this relationship that require further clarification. It has been suggested that alcohol and substance use have a role in precipitating anxiety and mood-related symptoms (8, 9). Their prevalent use in these populations raises the possibility that alcohol and other substances have a role in engendering or sustaining PTSD and comorbid symptoms (as well as use for self-medication). Additional fundamental questions regarding primary and secondary diagnostic relationships are raised by PTSD comorbidity. These include whether PTSD might represent a variation or specific expression of the other frequently associated anxiety or affective disorders or, conversely, whether depression, panic, phobic, or generalized anxiety symptoms develop as associated features or secondary complications of PTSD.

The phenomenology of co-occurring disorders has implications for their relationship to PTSD. A number of features that define PTSD such as emotional numbing, avoidance, and heightened arousal also characterize aspects of depression and phobic and panic disorders. In the definition of PTSD these features are usually linked to trauma-related stimuli. The patterns of occurrence of affective, phobic, and panic symptoms in combat veterans would therefore help to clarify their specificity to PTSD and trauma. In addition, symptom patterns that are considered to be endogenous in na-

ture, such as melancholia or spontaneously occurring panic attacks, would suggest a role for biological disturbances in combat veteran patients that overlap other clinical populations.

Temporal sequence of illness onset is also an important factor in defining relationships between primary and secondary illnesses. Course of illness has received much attention in other anxiety and affective disorders and has suggested mechanisms for illness progression (10-12). To our knowledge, the only study in the literature that has addressed sequence of illness onset in a veteran population with PTSD is that of Davidson et al. (5).

To obtain information on psychiatric conditions associated with combat-related PTSD, we recruited a clinical sample of veterans of high war zone stress from different military eras, including a group of former prisoners of war. In order to reduce potential confounds, we excluded patients with recent substance use disorders or severity requiring inpatient psychiatric treatment. In this report we provide information on the phenomenology and course of PTSD comorbidity in order to address the questions of whether comorbid symptoms appear specific to PTSD and trauma and whether there is a characteristic course for their emergence.

METHOD

Subjects

The majority of the patients were recruited from subjects consecutively referred to a newly established mental hygiene clinic PTSD program, primarily from Veterans Administration Medical Center clinical services. Additional subjects were established patients referred by other mental hygiene clinic clinicians who were familiar with the study's objectives and inclusion criteria. Patients were included if they had been in direct combat or high stress combat support roles, such as helicopter or field medic assignments, for a minimum of 3 consecutive months and/or had been prisoners of war. All of the included patients had also been repeatedly exposed to life-threatening situations and casualties. Patients were excluded if they had diagnoses of psychosis or dementia or had any other clinical signs of unreliable reporting. Patients were also excluded if they met criteria for alcohol or substance use disorder or had had a psychiatric inpatient admission within the past 2 years.

Procedure

Evaluations for screening and initial data gathering were conducted by a psychiatric social worker (C.A.R.). These assessments were semistructured and covered military histories, postmilitary social and occupational functioning, and family, social, and psychiatric histories. Information on experiences during combat and captivity was first elicited by open-ended inquiry, followed by establishment of the presence or absence of

specific stressors, including items on the Combat Exposure Scale of Lund et al. (13). Veterans Administration medical center records and military discharge forms were reviewed to verify service in a combat zone or captivity.

Psychiatric evaluation followed the initial assessment. After further review of military and family psychiatric histories, lifetime psychiatric diagnoses were determined by structured diagnostic interviews. These interviews used the Schedule for Affective Disorders and Schizophrenia—Lifetime Version (SADS-L) (14) to evaluate for Research Diagnostic Criteria and DSM-III-R anxiety, affective, and substance use disorders and to rule out psychotic disorders. Items were added to further address specific phenomenology and DSM-III-R hierarchical distinctions, which were conservatively applied. For example, the diagnosis of generalized anxiety disorder required a focus of worry other than war-related themes. The diagnosis of panic disorder was designated only if panic attacks occurred that were not provoked by specific stimuli, including reminders of combat, loud noises, interpersonal confrontations, or phobic situations. Phobic disorders were diagnosed for fear and avoidance of situations typical of phobias (e.g., crowded places, traveling distances, closed-in spaces, social scrutiny). The diagnosis of phobia also required that typical responses to the situations featured discomfort and/or anxiety and not the reexperiencing of trauma or fear of external threat. Since the SADS-L does not specifically evaluate PTSD criteria, a section from the Structured Clinical Interview for DSM-III-R, previously used to investigate PTSD (1), was added. If full or partial criteria for a disorder were established, patients were queried as to when the specific symptoms began. Additional questions addressed the subsequent course and severity of the disorder in question.

Psychiatric assessment also served to further evaluate for excluded conditions. In addition to diagnostic interviewing, patients were scrutinized for signs of pathological alcohol or drug use. Adequate recall ability in the World War II era veterans was confirmed by formal testing of address item recall and knowledge of major historical events and dates. Information from clinical records and the consistency of reporting within evaluations and clinical contacts were also considered. Patients were seen by the study team a minimum of three visits, and most were followed for subsequent treatment. Psychiatric evaluations were either conducted directly or supervised, with face-to-face follow-up interview, by the primary investigator (T.A.M.).

Data Analysis

Patients were grouped as those who had served in combat in Vietnam (Vietnam combat veterans) (N=27), those who had served in combat in World War II or Korea (non-Vietnam combat veterans) (N=18), and former prisoners of war (N=15) who also had served in World War II or Korea. Demographic and military history variables were compared between the groups; cate-

gorical variables were analyzed by chi-square analysis and continuous variables by analysis of variance. The number of patients who met lifetime criteria for a disorder were also compared between the study groups by chi-square analysis. The mean age at onset of the disorders found in sufficient numbers of subjects was compared to PTSD (which was the most prevalent disorder and, on average, the disorder of earliest onset) by paired t tests (two-tailed).

Characteristics of the Study Sample

Demographics. The average ages of the three groups were as follows: Vietnam combat veterans, 42.9 years (SD=3.6, range=38–57); non-Vietnam combat veterans, 67.4 years (SD=4.3, range=59–77); and former prisoners of war, 65.9 years (SD=4.5, range=58–71) ($F=123$, $df=2$, 59 , $p<0.001$). The Vietnam combat veterans group was more ethnically heterogeneous than the other two groups. Nineteen percent (N=5) were black and 37% (N=10) were Hispanic. The remaining Vietnam combat veterans (44%, N=12) and all but one Hispanic non-Vietnam combat veteran (6%) and one black former prisoner of war (7%) were white (Vietnam combat veterans versus non-Vietnam combat veterans versus prisoners of war: $\chi^2=18.5$, $df=4$, $p<0.001$).

Military stressors. Ninety-six percent of the 27 Vietnam veterans were assigned to Army (N=20) or Marine (N=6) infantry units where stressors included exposure to death and dismemberment of U.S. soldiers, fire from the enemy, sleep deprivation, and, in many, exposure to or responsibility for civilian casualties (81%). Sixty-seven percent of the non-Vietnam veterans (N=12, all Army) and 60% of the former prisoners of war (eight Army veterans and one Marine veteran) had also served in infantry units and endorsed a similar profile of combat stressors. Exposure to civilian casualties was somewhat less characteristic (50%) and possibly less extreme for the non-Vietnam combat veterans and former prisoners of war. Non-Vietnam combat veterans also included veterans of Navy combat in the Pacific theater (28%, N=5), and former prisoners of war included Air Force veteran flight combatants (33%, N=5). Statistical comparison of branch of service revealed Air Force ($\chi^2=12.5$, $df=2$, $p<0.05$) and Navy ($\chi^2=19.3$, $df=2$, $p<0.001$) service, but not Army ($\chi^2=0.9$, $df=2$, n.s.) and Marine ($\chi^2=5.7$, $df=2$, n.s.) service, to be differentially represented across the study groups.

In addition to combat stressors, former prisoners of war were often exposed to threats, physical abuse, deprivation of food and nutrition, and cold during captivity. The mean duration of captivity was 18.2 months (SD=7.1, range=7–33) and typically exceeded the duration of combat exposure before captivity. Thirty-three percent of the Vietnam combat veterans (N=9) and former prisoners of war (N=5) and 55% (N=10) of the non-Vietnam combat veterans had been wounded during combat ($\chi^2=1.96$, $df=2$, n.s.). Combat Exposure Scale scores were also comparable across the three groups (mean=4.9, SD=1.0 for Vietnam combat veter-

ans; mean=4.6, SD=1.0 for non-Vietnam combat veterans; mean=4.9, SD=1.1 for former prisoners of war) ($F=0.57$, $df=2$, 59, n.s.).

Psychosocial histories. On average, the patients had completed high school and some college. The Vietnam combat veterans tended to have had somewhat more education (Vietnam combat veterans: mean=14.0 years of school, SD=1.9; non-Vietnam combat veterans: mean=12.7 years, SD=2.1; prisoners of war: mean=12.5, SD=1.6) ($F=10.4$, $df=2$, 59, $p<0.001$). The majority of patients in all three groups were married at the time of evaluation (70%, $N=19$ of the Vietnam combat veterans; 67%, $N=12$ of the 18 non-Vietnam combat veterans; 73%, $N=11$ of the prisoners of war) ($\chi^2=0.18$, $df=2$, n.s.). During the past 10 years or 10 years before retirement age, the Vietnam combat veterans had been employed a mean of 75.9% (SD=33.2%) of the time, non-Vietnam combat veterans 67.4% (SD=4.3%), and former prisoners of war 82.9% (SD=28.9%) ($F=0.08$, $df=2$, 59, n.s.). Only one of the study patients, who had served in Vietnam, had a history of legal problems, and all were discharged from the military under honorable conditions.

Twenty-two percent of the total sample ($N=13$) reported histories strongly suggestive of psychiatric illness in immediate family members (seven Vietnam combat veterans, four non-Vietnam combat veterans, and two prisoners of war) ($\chi^2=1.4$, $df=2$, n.s.). An overlapping 30% ($N=18$) reported significant trauma before age 12, such as losing a parent through death or separation or having been abused or neglected (11 Vietnam combat veterans, four non-Vietnam combat veterans, and three prisoners of war) ($\chi^2=2.81$, $df=2$, n.s.).

Fifty-two percent ($N=31$) of the patients had received psychiatric treatment before contact with the study team. Treatment typically involved pharmacotherapy and supportive psychotherapy (received by 19 Vietnam combat veterans, seven non-Vietnam combat veterans, and five prisoners of war) ($\chi^2=0.24$, $df=2$, n.s.). Twenty-two percent of Vietnam ($N=6$) and non-Vietnam ($N=4$) combat veterans and none of the former prisoners of war had previous (remote) psychiatric hospitalizations ($\chi^2=0.68$, $df=2$, n.s.).

RESULTS

Prevalence of Disorders

The mean number of lifetime disorders per patient was 3.1 (SD=1.7, range=0 to 6). PTSD was the most prevalent lifetime disorder in the sample, with 82% ($N=49$) having met full criteria (table 1). The remaining 18% ($N=11$) of the patients reported symptoms that met criteria for one or two of the three diagnostic clusters for PTSD (see table 1, features column). Sixty-eight percent ($N=41$) of the sample also met full lifetime criteria for *DSM-III-R* major depression, 55% ($N=33$) for panic disorder, 53% ($N=32$) for generalized anxiety disorder, and 33% ($N=20$) for phobia. Subsyndromal

symptoms (i.e., those that did not meet full severity or duration criteria) were found for phobic disorders in an additional 27% of the sample, for obsessive-compulsive disorders in 20%, and for manic episode (hypomania) in 15%. Past histories that met criteria for alcohol or substance use dependence were elicited in 32% ($N=19$) of the patients. Each disorder was similarly represented in the three study groups (by chi-square comparisons) except for panic disorder. Two-way comparisons confirmed that panic disorder was underrepresented in the former prisoners of war ($N=17$, 63% of Vietnam combat veterans; $N=13$, 72% of non-Vietnam combat veterans; $N=3$, 20% of prisoners of war) (Vietnam combat veterans versus prisoners of war: $\chi^2=13.6$, $df=1$, $p<0.01$; non-Vietnam combat veterans versus prisoners of war: $\chi^2=9.2$, $df=1$, $p<0.01$; Vietnam combat veterans versus non-Vietnam combat veterans: n.s.).

Features

Of the 11 patients who had "partial" PTSD, nine met the criteria for the disorder except for *DSM-III-R* cluster C (symptoms of numbing and withdrawal). The remaining two patients with partial PTSD were both former prisoners of war and reported symptoms that met criteria *only* for numbing and withdrawal.

Criteria for melancholic type were present in 34% ($N=14$) of the 41 patients with major depression for a minimum of 2 consecutive weeks during the course of the condition. Patients who met full or subthreshold diagnostic criteria for panic disorder by definition experienced attacks that were unprovoked in nature. Seventy-one percent ($N=27$ of 38) of these patients' panic attacks included episodes that were reported to awaken them from sleep without dream recall. In 78% ($N=28$) of the 36 patients with phobic symptoms, the predominant phobic situations included crowded places. Other common phobic situations were social (being a focus of attention: 31%, $N=11$), traveling distances (19%, $N=7$), and closed-in spaces (three former prisoners of war, 8%). One veteran, who had been in a helicopter crash, developed a marked fear and avoidance of elevators. The predominant obsessive-compulsive symptoms were excessive checking behaviors in 71% ($N=10$) and ego-alien aggressive thoughts in 29% ($N=4$) of the 14 affected patients.

Onset

In all but one of the patients the original onset of PTSD symptoms was acute by the *DSM-III-R* definition (within 6 months of the stressful experience). One patient reported a history of childhood separation anxiety, and another reported the onsets of generalized anxiety disorder and major depression in late childhood and alcohol abuse in adolescence. Otherwise, the onsets of disorders were reported to have been proximate to, or sometime after, combat exposure.

The comparisons of mean age at illness onset include the comorbid conditions adequately represented and

TABLE 1. Lifetime Prevalence of PTSD and Related Psychiatric Disorders in Combat Veterans

DSM-III-R Diagnosis	Total (N=60)				Vietnam Veterans (N=27)				World War II and Korean War Veterans							
			Met Sub-threshold Criteria				Met Sub-threshold Criteria		Non-POWs (N=18)				POWs (N=15)			
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
PTSD	49	82	11	18	25	93	2	7	14	78	4	22	10	67	5	33
Major depression	41	68	6	10	21	78	2	7	12	67	1	6	8	53	2	13
Panic disorder	33	55	5	8	17	63	2	7	13	72	3	18	3	20	1	7
Generalized anxiety disorder	32	53	2	3	15	56	1	4	9	50	1	6	8	53	0	0
Phobia	20	33	16	27	11	41	10	37	7	39	3	17	2	13	3	20
Alcohol/substance use dependence	6	10	13	22	2	7	8	30	3	17	2	11	3	20	1	7
Obsessive-compulsive disorder	2	3	12	20	1	4	7	26	1	6	3	17	0	0	2	13
Manic episode	0	0	9	15	0	0	5	19	0	0	2	11	0	0	2	13

cases in which at least an approximate time of symptom onset was recalled. Onset of panic disorder (mean=31.3 years; $t=4.5$, $df=37$, $p<0.001$), major or minor depression (mean=30.0; $t=4.2$, $df=46$, $p<0.001$), and phobia or phobic symptoms (mean=27.6; $t=2.9$, $df=35$, $p<0.01$) was later than onset of PTSD (mean=23.2) (table 1), in contrast to generalized anxiety (mean=24.3 years; $t=0.94$, $df=33$, n.s.) and alcohol/substance use disorders (mean=25.4; $t=1.4$, $df=18$, n.s.). Similar relationships of onsets of illnesses were found for comparisons made within the study subgroups.

Subsequent Course

DSM-III-R PTSD symptoms per se, particularly those involving the reexperiencing of trauma, were reported to have significantly diminished in frequency and intensity from the first year or several years after combat or captivity in 45% (N=27) of the total study sample. In the remaining 55% (N=33), PTSD symptoms had been persistent or recurrent. Depression and generalized anxiety disorders were even more frequently described as persistent or recurrent; only 19.5% (N=8) of the patients with major depression and 6.0% (N=2) of the patients with generalized anxiety disorder reported discrete, time-limited episodes. The frequency of panic attacks varied episodically. While phobias and obsessive-compulsive symptoms were typically not severe, they were persistent in virtually all of the affected patients. Among the patients who met criteria for past alcohol or substance abuse or dependence, pathological use of alcohol or substances was reported to have been absent for a mean 12.1 years (SD=11.4, range=3-40). Several of these patients reported that discontinuation was associated with exacerbations of other symptoms.

DISCUSSION

The study sample in the present study consisted of symptomatic veterans whose lifetime psychiatric morbidity was initially provoked or significantly affected by severe, war-related stress. Consistent with previous studies (1-7), we found a high frequency of typically persistent anxiety and affective symptoms in association with PTSD in our study subjects. Our findings further suggest that these psychiatric conditions phenomenologically overlap other clinical populations; however, the pattern of occurrence of some specific symptoms also suggests a relationship to trauma. In addition, the ubiquitous presence of lifetime symptoms of PTSD and certain observations on course of illness are consistent with the hypothesis that PTSD represents a primary pathogenic process.

We found, similarly to a study of victims of civilian disasters (15), that among PTSD symptoms, numbing and withdrawal occur more variably than reexperiencing and heightened arousal. Persistent numbing and withdrawal in two former prisoners of war, who had little other psychiatric morbidity, suggests that restricting emotions and avoidance behavior may be partially adaptive for some patients. Panic and major depression were, on average, the disorders most delayed in onset compared to PTSD and also emerged somewhat later than the median age at onset (23 years) for both disorders in men that was reported in the Epidemiologic Catchment Area study (16). These observations on course of illness suggest that panic and depression, as they occur with PTSD, can represent secondary complications and manifestations of illness progression. Conversely, the relatively early emergence of generalized anxiety disorder suggests that symptoms of the disorder

TABLE 1 (continued)

Age at Onset (years)			Features
Mean	SD	Range	
23.2	4.0	18-37	Nine (15%) met <i>DSM-III-R</i> criteria A, B, and D only; two (3%) met criteria A and C only
30.0	12.3	12-69	Fourteen (30%) had lifetime melancholia
31.3	12.0	19-67	Twenty-seven (70%) had panic attacks during sleep
24.3	6.0	12-43	
27.6	10.3	7-61	Twenty-eight (78%) had phobia of crowded places, 11 (31%) of social situations, seven (19%) of traveling distances, and three (8%) of closed-in spaces
25.4	7.3	15-44	
24.3	5.3	16-34	Ten (71%) experienced excessive checking, four (29%) aggressive thoughts
26.5	6.0	20-35	Hypomania

der, like PTSD, may represent a primary response to trauma.

Our findings are limited by their retrospective nature. One recall bias could be a tendency to link symptom onset to dramatic life events. This would not account for finding certain conditions to be delayed in onset relative to PTSD, however. We further believe that the exclusion of patients with recent pathological substance use and the focus on a relatively functional outpatient sample enhanced the reliability of reported information. In addition, the comparable degree of psychosocial risk factors and military stress, excluding captivity, and comparable comorbidity profiles between our study groups support the validity and some generalizability of these findings. The sequence of onset of psychiatric conditions in our study is quite similar to the findings of Davidson et al. (5). The relative prevalence of disorders in our sample is also similar to the aforementioned study, which also recruited outpatient veterans of Vietnam and World War II combat (5). We also found a lifetime prevalence of PTSD in the prisoners of war which was similar to that reported in a recent study of former prisoners of war recruited through outreach sources (67% versus 50%) (17). The prevalence of major depression and panic disorder in the Vietnam veteran subgroup, however, exceeds the rates of co-occurrence with PTSD documented in a community-based sample of Vietnam veterans in the National Vietnam Veterans Readjustment Study (78% versus 26% and 63% versus 8%, respectively). The corresponding rates for generalized anxiety disorder were more comparable (56% versus 44%). Thus, our findings appear to be representative of a relatively symptomatic and chronic, albeit functional, subgroup of veterans with psychiatric morbidity related to war trauma.

Symptom patterns that are considered markers of endogenous disturbances (e.g., "spontaneous" panic attacks, major depression, melancholic features) were common in our sample. In fact, the percent of the PTSD patients with comorbid panic who reported attacks during sleep (70%) is almost identical to the prevalence of panic attacks during sleep in a panic disorder population (69%) (18). One explanation for these observations is that factors which predispose individuals to affective and other anxiety disorders may have a role in influencing susceptibility to PTSD. An alternative but not mutually exclusive possibility that is consistent with epidemiologic data (7) is that trauma and PTSD influence the concurrent or delayed emergence of other psychiatric disturbances. Progression of illness from symptoms specific to PTSD, in which anxiety is evoked by trauma-related or startling stimuli, to phobic situations, to spontaneous panic attacks suggests a process in which symptomatic responses occur increasingly autonomously. Such a process is consistent with the model of electrophysiologic kindling, which has been postulated to be involved in PTSD (19) as well as in affective illness (10) and in panic attacks associated with cocaine use (9). It is also possible that evolving disturbances in neurotransmitter functioning may underlie PTSD and the emergence of co-occurring conditions. Some studies have suggested increased noradrenergic activity in PTSD (20, 21). Chronic overactivity might effect secondary and tertiary changes of neurotransmitter depletion and sensitization of receptor subsystems. Such dysregulation of the noradrenergic system has been invoked in depression and panic disorder (22, 23). It has also been suggested that hypertension is a potential consequence of heightened noradrenergic activity related to sympathetic arousal in populations with PTSD (24). It is therefore of interest that we have recently found that 53% of an overlapping PTSD group (70% in non-Vietnam era, 32% in Vietnam era patients) met criteria for hypertension, compared to 31% of a VA psychiatric comparison group of similar age and cardiovascular risk profile (O. Brawman-Mintzer, N. Hernandez, T. Mellman, unpublished observations).

The implication that mechanisms underlying PTSD comorbidity overlap other psychiatric disorders requires validation from studies of biological markers and treatment response. The possibility that disturbances which are thought to be genetically influenced might also be acquired through extreme stressors and subsequent responses to stress is, however, intriguing. The observations of specific symptom patterns that overlap other clinical populations but are also consistent with traumatic influence support such a hypothesis. For example, the relative predominance of the phobic symptom of fear of crowded places suggests a conditioning effect of combat, as do other associations of phobias with specific experiences (e.g., claustrophobia in three former prisoners of war, an elevator phobia in a helicopter crash survivor). Obsessive-compulsive disorder features of excessive checking behaviors and ego-alien aggressive thoughts also appear to be themati-

cally related to combat experiences. The finding that panic was relatively underrepresented in the former prisoners of war group may mirror the finding of Green et al. (25), who reported a positive association between panic disorder and past special combat assignments in Vietnam. Panic disorder is characterized by anxiety attacks that at times occur unpredictably. It is likely that special combat assignments featured unpredictable patterns of stress more typically than did captivity during World War II.

The association of other psychiatric disorders with PTSD is an important consideration in accounting for the chronicity that has been found in PTSD populations and in conceptualizing treatment strategies. From a more general perspective, it would appear that patterns of response to trauma have implications for a range of psychiatric phenomena.

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Recovery and Relapse From Major Depressive Disorder in the Elderly

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Objective: Results from the National Institute of Mental Health (NIMH) Collaborative Study of the Psychobiology of Depression raised serious concerns about the longer-term prognosis for major depressive disorder in younger persons. However, little research has examined the prognosis for major depressive disorder in the elderly despite suggestions that they have poorer clinical outcomes than younger adults. The objective of this study was to 1) document rates of recovery and relapse from major depressive disorder in a large group of inpatient elderly and 2) compare recovery and relapse rates from major depressive disorder in the elderly with those in a mixed-age patient group from the NIMH collaborative study. **Method:** The psychiatric status of 127 elderly inpatients diagnosed with major depressive disorder by Research Diagnostic Criteria was evaluated for 1 year. The same diagnostic and follow-up methods to assess psychiatric symptoms employed in the NIMH study were used. **Results:** One year after study admission, 72% of elderly patients had recovered. Nineteen percent of recovered patients, however, had a subsequent episode of major depressive disorder. Recovery and relapse rates in the elderly did not significantly differ from those reported for the mixed-age group in the NIMH study. **Conclusions:** It is erroneous to single out the elderly as being more likely to have poorer longitudinal treatment outcomes than others. Study findings indicate the need for continued refinement of somatic and nonsomatic treatments for the elderly to improve rates of sustained recovery from depression.

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In the last decade results from a series of studies sponsored by the National Institute of Mental Health (NIMH) raised serious concerns about the longer-term efficacy of established treatments for depression. Using multicenter data from the NIMH Collaborative Study of the Psychobiology of Depression (1), Keller and Shapiro (2) indicated that prognosis for major depressive disorder in a mixed-age population treated in an uncontrolled (naturalistic) fashion was modest. While three-quarters of the patients recovered within 1 year, over one-third of those who recovered subsequently relapsed. The mean age of the patients was 35.5 years, however, and it is unclear whether comparable rates of recovery from and relapse into major depressive disorder would be found in a group of elderly subjects.

While findings from the NIMH collaborative study alerted many to possible limitations of existing treatments, those delivering mental health services to the elderly have had long-standing concerns about the longitudinal efficacy of treatments for depression in this group. Early research (3, 4) suggested that the prognosis was poor for the depressed elderly, and some clinicians held modest treatment expectations for older patients. Findings from the NIMH study of depression suggested the possibility that poor longitudinal treatment outcomes may not be confined to the elderly but may reflect larger problems in how to optimize the treatment of depression. Nonetheless, age may be related to different treatment outcomes. An answer to this question, however, requires a direct comparison of longitudinal outcomes, using the same methodology, between older and younger patients.

Two longitudinal, naturalistic follow-up studies of depressed elderly subjects appeared after initial findings from the NIMH collaborative study were reported. They drew two different conclusions about the course of major depressive disorder in older patients. The view that the prognosis for depression in the elderly is poor was supported by Murphy (5), who found that only one-third of older depressed patients had a good outcome after 1 year of psychiatric treatment. In contrast, Baldwin and Jolley (6) reported that almost

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three-fifths of a group of depressed elderly they studied were well 1 year after hospital admission. Methodological differences between the two studies may have explained the variance in outcomes. Unfortunately, comparison of results from these two studies with those from the NIMH collaborative study was difficult, since they used different diagnostic and follow-up procedures. The question of whether the prognosis for depression differs in the elderly and in younger age groups thus remains to be addressed despite recent calls for research on this topic (7).

The present research longitudinally studied for 1 year a group of elderly patients who were psychiatrically hospitalized with major depressive disorder. The same diagnostic and follow-up methods to assess psychiatric symptoms employed in the NIMH collaborative study of depression were used. The goals of this report are to 1) document rates of recovery and relapse among a group of inpatient elderly with major depressive disorder and 2) compare recovery and relapse rates in the elderly with those found in a mixed-age group of patients from the NIMH study.

METHOD

Sample

Baseline. Persons 60 years or older, admitted to the psychiatric inpatient service of a hospital, who met Research Diagnostic Criteria (RDC) (8) for major depressive disorder, participated in the study. Patients were not included if they had a documented history of bipolar disorder, schizophrenia, or neurological deficits or evidenced an organic brain syndrome or disorder. Since the research was part of a larger study of family issues in late-life depression (9), patients eligible for the study were required to have an involved spouse or adult child. Patients were interviewed with the Schedule for Affective Disorders and Schizophrenia (SADS) (10). A total of 150 patients agreed to take part in the research; they represented 84% of those who were eligible for the study. Informed consent was obtained from participants after study procedures were explained. During psychiatric hospitalization, which lasted a mean of 6.5 weeks ($SD=3.6$), elderly patients were treated in an uncontrolled fashion with antidepressant medications and/or ECT.

Follow-up. At 6 months and 1 year after hospital admission, older patients and their respective family members were interviewed by using the psychiatric status ratings from the Longitudinal Interval Follow-Up Evaluation (11) and other indices that characterized their psychiatric condition. Among the original group of 150 patients, data on longitudinal psychiatric status were successfully gathered on 127 patients (85%). Of patients for whom follow-up data were not obtained (and who were therefore not included in these analyses), five (3%) had died, 16 (11%) refused interviews, and two (1%) could not be reached. There were no sig-

nificant demographic or clinical differences between those who remained in the study and those from whom we were unable to collect follow-up data.

Study Measures

Baseline. Demographic information gathered on patients included sex, marital status, age, race, religion, and socioeconomic status, measured by the Four Factor Index of Social Status (12). Descriptors of the patient's past and current psychiatric history were derived from the SADS. The interviews for the SADS and Longitudinal Interval Follow-Up Evaluation (discussed later) were conducted by one research staff member with extensive training in the administration of these instruments. All study diagnoses and Longitudinal Interval Follow-Up Evaluation ratings were reviewed by the author. These included age at onset of major depressive disorder; history of prior episodes of major depressive disorder; duration of index episode of major depressive disorder; whether the index episode was superimposed on a chronic depression ("double depression") (13); severity of depression, rated with an equivalent of the Hamilton Rating Scale for Depression (14); and whether the index episode had psychotic features. A staff rating of the patient's physical health status was also obtained.

Follow-up. Follow-up assessments were made by using the psychiatric status ratings from the Longitudinal Interval Follow-Up Evaluation. The psychiatric status ratings were used to evaluate the prior 6 months of the patient's psychiatric condition. The course of psychopathology was then recorded by using a rating system linked to the RDC. On the basis of explicit Longitudinal Interval Follow-Up Evaluation criteria, recovery was defined as 8 continuous weeks in which the patient evidenced no or minimal symptoms of depression. Patients were classified as relapsed if they had recovered from the index episode of major depressive disorder and subsequently met the RDC for another episode of major depressive disorder during the 1 year period after admission to the study. A complete description of the Longitudinal Interval Follow-Up Evaluation methodology has been detailed elsewhere (11). During each 6-month follow-up assessment, the following information was also obtained: 1) scores on the SADS-derived measures of functional impairment secondary to the patient's psychiatric condition; 2) scores on the SADS Global Assessment Scale; 3) Global Improvement Scale scores; 4) emergence of suicidal behavior; and 5) the patient's characteristic treatment status.

RESULTS

About two-thirds of the patients in this study were married and widowed women. The vast majority (97%) were white. As can be seen in table 1, most patients were Jewish or Catholic, occupied middle levels of social status, and had an average age of 71 years.

TABLE 1. Demographic and Clinical Characteristics of 127 Elderly Depressed Patients

Characteristic ^a	N	%
Sex		
Male	38	30
Female	89	70
Marital status		
Married	77	61
Widowed	43	34
Divorced/separated	7	5
Social class status ^b		
Major business, professional	11	9
Medium business, minor professional	41	34
Skilled craftworkers, clerical, sales workers	38	31
Machine operators, semiskilled workers	25	21
Unskilled laborers, manual service workers	6	5
Religion		
Protestant	11	9
Catholic	42	33
Jewish	74	58
Onset of major depressive disorder		
Before age 50	35	27
At or after age 50	92	73
Prior episodes of major depressive disorder		
No	37	29
Yes	90	71
Median weeks' duration of index episode at admission	15	
Index episode superimposed on chronic depression ^b		
No	113	91
Yes	11	9
Psychotic depression		
No	101	80
Yes	26	20
Patient's physical health ^b		
Very poor/poor	16	13
Fair	31	24
Good/excellent	79	63

^aThe mean age of the patients was 70.9 (SD=6.8), and the mean equivalent Hamilton depression score was 24.5 (SD=5.7).

^bData not available for all subjects.

Almost three-quarters of the patients had an onset of major depressive disorder after age 50, and a similar proportion had had prior episodes of major depressive disorder. As reflected in the mean Hamilton equivalent score of 24.5, patients were severely depressed at admission, with episodes that had lasted a median of almost 4 months. One-fifth had psychotic depressions, and 9% had an index episode that was superimposed on a chronic depression. The majority of older patients were in fair to excellent physical health.

Recovery and Relapse at 1 Year

Clinical outcomes for this study (and those from the NIMH collaborative study) are summarized in tables 2 and 3. Table 2 reports the proportion of patients who recovered and relapsed over 1 year from study admission. Table 3 provides a general characterization of the patients' psychiatric condition over 1 year, including information about the presence of concurrent psychiatric symptoms among patients classified as recovered. Summarizing data in these two ways facilitated comparison

TABLE 2. Recovery and Relapse at 1 Year of Elderly Depressed Patients in the Present Study and of a Mixed-Age Group in the NIMH Collaborative Study of Depression

Item	Present Study (N=127)		NIMH Study (2) (N=101)	
	N	%	N	%
Patient recovered from index episode of major depressive disorder				
No	35	28	26	26
Yes	92	72	75	74
If index episode ended, relapse into major depressive disorder ^a				
No	74	81	59	79
Yes	17	19	16	21
If index episode ended, relapse into diagnosable affective episode ^{a,b}				
No	70	77	48	64
Yes	21	23	27	36

^aRelapse rates calculated only on those subjects who recovered. Data not available for one subject in the present study.

^bFor the present study, diagnoses included major depressive disorder (N=17) and RDC-defined minor depressive disorder (N=4); for the NIMH study, diagnoses included major depressive disorder (N=16), minor depressive disorder (N=7), mania (N=2), and hypomania (N=2).

of this study's findings with those derived from the NIMH study.

As can be seen in table 2, 72% of study participants recovered from the index episode of major depressive disorder by 1 year from date of hospital admission. Nineteen percent of those who recovered subsequently developed an additional episode of major depressive disorder within 1 year from admission. A higher proportion (23%) relapsed into any diagnosable affective episode (i.e., major depressive disorder or minor depressive disorder). The general characterization of all study participants over the course of 1 year (summarized in table 3) indicates that 59% recovered from the index episode of major depressive disorder and did not relapse into another episode, 13% recovered but later relapsed into major depressive disorder, and 28% did not recover during the year study period. It is noteworthy that 31 (42%) of the 74 patients classified as having fully or partially sustained recovery nonetheless experienced nondiagnosable affective symptoms or minor depressive disorder in the period after recovery from the index episode.

Other findings from this research (not presented in tables) indicated that at 1 year after entry into the study, 63.5% of study patients were judged much or very much improved, 36% still had at least some functional impairment due to psychiatric illness, and 8.7% had made (unsuccessful) suicide gestures or attempts and that Global Assessment Scale scores improved from an index episode average of 38.0 (SD=8.4) to 69.3 (SD=15.4). Further, the characteristic treatment status of study patients in the year-long follow-up was as follows: 10.2% not in treatment, 86.7% in outpatient psychiatric treatment, and 3.1% psychiatrically hospitalized.

TABLE 3. Clinical Status Over One Year of Elderly Depressed Patients in the Present Study and of a Mixed-Age Group in the NIMH Collaborative Study of Depression

Item	Present Study (N=127)		NIMH Study (2) (N=101)	
	N	%	N	%
Fully or partially sustained recovery from index episode ^a	74	59	59 ^b	58
No relapse	43	34	30	30
Minor affective symptoms	27	22	18	18
Minor depressive disorder	4	3	7	7
Mania/hypomania	—	—	4	4
Remission/relapse with same condition as in index episode	17	13	16	16
No recovery	35	28	26	26

^aData not available for one subject in present study.

^bFour subjects with mania/hypomania are classified as recovered (i.e., no subsequent episode of major depressive disorder) to facilitate comparison of findings.

Comparison of Findings With the NIMH Collaborative Study of Depression

Comparison of this study's findings with NIMH collaborative study results reported by Keller and Shapiro (2) offers a particularly valuable opportunity, since both used the same diagnostic and psychiatric follow-up methods. The two studies differed, however, on several demographic and clinical descriptors. Patients in the present study were more likely to be currently married and female than were those in the study of Keller and Shapiro (2). All of the patients in the present study had a diagnosis of major depressive disorder and were hospitalized, whereas 25% of the patients described by Keller and Shapiro were outpatients and had bipolar disorder. In addition, the duration and severity of the index episode were less, and fewer patients had superimposed depression than those who participated in the collaborative study of depression. Number of prior episodes and proportion of patients with psychotic depression were comparable in the two study groups.

As seen in table 2, there were no significant differences between the two studies on recovery from the index episode of major depressive disorder ($\chi^2=0.01$, $df=1$, n.s.) or relapse into another major depressive disorder among those who recovered ($\chi^2=0.05$, $df=1$, n.s.). Of the two studies, a higher proportion of Keller and Shapiro's participants (2) developed diagnosable affective episodes (36% versus 23%); however, the difference was not statistically different ($\chi^2=2.74$, $df=1$, n.s.).

Findings in table 3 reveal no differences between the two studies in a general characterization of the psychiatric condition of patients as fully or partially recovered (present study: 59%, Keller and Shapiro: 58%), remitted with relapse into same condition as index episode (13% versus 16%), or not recovered (28% versus 26%) ($\chi^2=0.31$, $df=2$, n.s.). Similar to findings from the present study, in Keller and Shapiro's study 29 (53%) of 59 patients classified as having fully or partially sus-

tained recovery evidenced minor affective symptoms or diagnoses after recovery.

DISCUSSION

In this study 72% of elderly inpatients recovered from an episode of unipolar major depressive disorder within 1 year. However, 19% of those who recovered subsequently relapsed into another episode of major depressive disorder. Rates of recovery and relapse did not significantly differ from those found in a mixed-age population of the NIMH collaborative study of depression (2) that used the same diagnostic and follow-up methodology.

While this research found that the majority (59%) of older adults did recover from an episode of major depressive disorder and did not relapse into another episode, over two-fifths of the recovered subjects subsequently experienced nondiagnosable affective symptoms or, less often, minor depressive disorder. Keller and colleagues (15) have suggested that one reason for the modest clinical psychiatric outcomes they found in a mixed-age population is that patients are not treated with sufficiently high doses of antidepressant medication. Our findings underscore, however, that it is erroneous to single out the elderly as being more likely to have poor treatment outcomes from major depressive disorder, since their recovery and relapse rates are comparable to those in a group of predominantly younger individuals.

There are two limitations of a comparison of this study's findings with those reported by Keller and Shapiro (2). The first is that the two study groups differed regarding several demographic and clinical characteristics. It is possible that these differences were related to recovery and relapse. Only one of the variables on which there was a significant difference between the two study groups, duration of episode, was in fact related to poorer outcome by Keller and Shapiro (2). A reexamination of data from this study, however, found no relationship between any of the demographic and clinical descriptors on which the two study groups differed and recovery or relapse in the elderly. Future comparisons between mixed-age and elderly patients will most likely also continue to find demographic and clinical differences between these two groups. Demographic descriptors change as a function of age (e.g., sex differences in life expectancy result in increasing proportions of women in later life), as do clinical descriptors (e.g., older persons have more years at risk for episodes of psychiatric illness than younger persons). One factor that was not systematically assessed in this research but should be in future studies is types of treatment received, since treatment differences may be related to clinical outcomes.

The second limitation is that only patients with involved spouses or adult children were included in the present study. If family involvement in care of a depressed individual were related only to better clinical outcomes, our findings might be portraying a more fa-

avorable response to treatment than would have been found in a sample that included never-married persons or ever-married individuals without family support. A large body of research on patients with schizophrenia and depression indicates, however, that family members can have both positive and negative effects on the course of psychiatric illness in their patient relatives (16).

It is difficult to directly compare this study's findings with those of Murphy (5) and with Baldwin and Jolley's widely cited follow-up studies of the depressed aged (6) because of their different diagnostic and follow-up procedures. A general comparison of their results with those of the present study and Keller and Shapiro's study (2) is nonetheless informative since Murphy (5) and Baldwin and Jolley (6) conducted 1-year, naturalistic, follow-up studies. If patients who died or developed dementia are excluded from Baldwin and Jolley's and Murphy's outcome data, 67 of 103 patients (65%) in Murphy's study and 72 of 90 patients (80%) in Baldwin and Jolley's study recovered from an index episode. These results do not significantly differ from those of the present study and those of Keller and Shapiro (2) ($\chi^2=5.53$, $df=3$, n.s.). In Baldwin and Jolley's study, 26 of 72 patients (36%) who recovered later relapsed into an episode of depression—a rate significantly higher than that in the present study and in Keller and Shapiro's ($\chi^2=7.25$, $df=2$, $p<0.05$). It was not possible to calculate a relapse rate from Murphy's published data that allowed comparison with the other studies, since her definition of "recovered" patients may have included those who relapsed but who again recovered by the end of 1 year. It therefore appears that with respect to recovery rates, there is convergence of outcomes among these four different studies.

In conclusion, these findings indicate that there is considerable similarity in treatment outcomes for elderly and younger patients treated in an uncontrolled fashion. Therapeutic pessimism based on age is unwarranted. Nonetheless, many patients in this study and in the NIMH collaborative study continued to evidence problems with depression in the year from study entry. These data indicate the need for continued development and refinement of somatic (17) and nonsomatic (18) treatments for the elderly that will increase the proportion of patients with sustained recovery from depression.

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Prediction of Outcome in Mania by Mood-Congruent or Mood-Incongruent Psychotic Features

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Objective: The aim of this study was to determine the significance of mood congruence of psychotic features in mania as a predictor of outcome. **Method:** Fifty-four patients with bipolar disorder were followed prospectively for 4 years after recovery from an episode of mania with psychotic features. Assessments of residential and occupational status, interepisode symptoms, and episode recurrences were made at 6 and 48 months after recovery. Categorical outcomes were evaluated by logistic regression and recurrence risk with survival analysis. **Results:** Mood-incongruent psychotic features during the index manic episode predicted a shorter time in remission at 4 years (hazard ratio=2.6), and Schneiderian first-rank symptoms predicted poor residential status at 4 years (odds ratio=20.1). **Conclusions:** Differentiation of mood congruence of psychotic features in mania evidently has prognostic validity and, therefore, has utility as a nosological characteristic.

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Presence or absence of psychotic features is a common basis for subdividing major affective syndromes. In *DSM-III-R* the fifth digit in the code number allows for the classification of manic episode with psychotic features and severe manic episode without psychotic features as well as the distinction of mood-congruent and mood-incongruent psychotic features. Traditionally, mood congruence has been associated with mood disorders and mood incongruence has been associated with schizophrenia, although *DSM-III* and *DSM-III-R* proposed that mood incongruence can occur in affective disorders. This tentative proposal requires validation.

Many investigators have tried to validate subtypes of affective disorders with follow-up studies. Specifically, the presence of psychotic features as a predictor of outcome in mania has been considered (1-10). Coryell et

al. (7) found that loosening of associations in a group of patients with psychotic and schizoaffective mania predicted a worse outcome at 5 years. Rosen et al. (6) found that patients with psychotic bipolar disorder showed poorer social functioning than patients with nonpsychotic bipolar disorder. Furthermore, Rosenthal et al. (5) found that patients with psychotic mania had longer periods of remission while receiving maintenance lithium treatment than did patients with nonpsychotic mania. Others (1-4, 8) have found no difference in outcome on the basis of the presence of psychotic features.

Several studies (11-18) have looked specifically at mood congruence of psychotic features in affective disorders in relation to outcome. Coryell and Tsuang (11) found that depressed patients with mood-incongruent features were younger and had a poorer outcome at 2-3 years but no difference at 40 years. Brockington et al. (16) found that manic patients with mood-incongruent psychotic features had a worse outcome than manic patients without psychotic features and manic patients with mood-congruent psychotic features. A recent report by Miklowitz et al. (17) indicated that "classical schizophrenic symptoms" have a prognostic utility in bipolar disorders. Abrams and Taylor (18), however, found no difference in outcome between patients with mood-congruent and mood-incongruent psychotic affective disorder. Kendler (19) recently published an empirical review of mood-incongruent psychotic affective illness. On the basis of a methodologically sound literature review, he concluded that mood-incongruent psychotic affective illness most likely represents a subtype

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of affective disorder, as proposed in *DSM-III-R*, rather than a form of schizophrenia or a separate disorder.

Comparisons of such studies are complicated by variable definitions of "psychotic features." In their comprehensive book on manic-depressive illness, Goodwin and Jamison (20) summarized 26 studies of psychotic features in mania and reported that the prevalence ranged from 47% to 75% of patients with bipolar disorder at some time in the course of their illness and that the rate tended to decline with increasing age of onset. Black and Nasrallah (13) found psychotic features in 44% of 467 patients with bipolar disorder; 28% of the patients had mood-congruent psychotic features and 9% had mood-incongruent psychotic features. Kendler (19) called for more studies of mania that address the validity of mood congruence of psychotic symptoms.

We have previously reported that the presence of psychotic features in mania predicts poor outcome, including higher risk of relapse and poor psychosocial outcome (9, 10). We now report the significance of mood congruence of psychotic features as a predictor of outcome in mania.

METHOD

The present study involved a 4-year follow-up of 54 patients with bipolar disorder who, during their index episode, experienced mania with psychotic features. These 54 patients were drawn from a larger pool of subjects with psychotic and nonpsychotic mania in a study reported elsewhere (9). Most of the 54 patients in the current study were young, middle-class, and unmarried (table 1). Fifteen (27.8%) had had no previous episodes of mania. Their mean age was 30 years ($SD=9.5$). A *DSM-III* diagnosis of mania was obtained by using the National Institute of Mental Health Diagnostic Interview Schedule (DIS) (22). All of the patients were at least 17 years of age, had recovered from the index manic episode at entry into the study, and provided informed consent. Recovery was defined operationally as reported elsewhere (9). Treatment was not under the control of the investigators.

At entry into the study, 30 (55.6%) of the patients had mood-incongruent features and 24 (44.4%) had mood-congruent psychotic features (table 1). We identified eight individuals with predominantly grandiose delusions but who also had persecutory delusions. We classified these patients as having mood-congruent psychotic features. In addition, we conducted a second analysis including them with the mood-incongruent group.

Psychotic features were defined according to *DSM-III-R* as the presence of either delusions or hallucinations or behavior so grossly disorganized that "a reasonable inference can be made that reality testing is markedly disturbed." Psychotic features were divided as to their mood congruence or incongruence according to *DSM-III-R* definitions and DIS data obtained by one

TABLE 1. Demographic Characteristics and Type of Psychotic Features at Index Manic Episode of 54 Patients With Bipolar Disorder Who Had Psychotic Mania

Item	N	%
Demographic characteristics		
Sex		
Women	30	55.6
Men	24	44.4
Marital status		
Married	16	29.6
Not married	38	70.4
Socioeconomic status ^a		
Lower	4	7.4
Middle	34	63.0
Upper middle and upper	16	29.6
Type of psychotic features		
Mood-congruent ^b	24	44.4
Mood-incongruent ^b	30	55.6
First-rank symptoms	11	20.4
Paranoid delusions ^c	35	64.8
Bizarre delusions	9	16.7
Auditory hallucinations	16	29.6
Visual hallucinations	5	9.3

^aHollingshead criteria (21).

^bTwelve patients had both mood-congruent and mood-incongruent features; these patients were classified as having mood-congruent or mood-incongruent features depending on which type of feature predominated.

^cEight of the patients with paranoid delusions had predominantly mood-congruent delusions but also had nongrandiose paranoid delusions that were less prominent or milder.

of us (M.T.). Delusions and hallucinations were considered mood congruent when their content was consistent with a manic mood, such as "themes of inflated worth, power, knowledge, or identity or a special relationship to a deity or a famous person" (*DSM-III-R*). Psychotic features were considered mood incongruent if they did not involve such manic themes and included nongrandiose persecutory delusions, thought insertion, thought broadcasting, delusions of being controlled, or catatonic features. Patients who had both mood-congruent and mood-incongruent psychotic features ($N=12$) were assigned to the type that seemed to predominate.

Patients also were classified as having or lacking Schneiderian first-rank symptoms (23), which were considered mood-incongruent features according to the *DSM-III* definition. Mood-incongruent psychotic mania was differentiated from schizoaffective mania according to *DSM-III-R* definitions. For mania, the mood-incongruent features had to be restricted to periods of a full affective syndrome. In contrast, according to Research Diagnostic Criteria (24), the presence of certain psychotic features during a manic episode in an individual with good premorbid adjustment would qualify that individual for a diagnosis of a schizoaffective disorder.

To assess the reliability of the distinction between presence or absence of mood congruence and first-rank symptoms, an independent rater (D.C.G.) reviewed the medical records blind to the index assessment. Categorical correlations of the two raters were high (six disagreements out of a total of 54 assessments in both

TABLE 2. Prediction of Psychosocial Outcome 4 Years After Recovery for 54 Patients With Bipolar Disorder Who Had Psychotic Mania

Predictor	Poor Residential Status ^a		Poor Occupational Status ^b	
	Adjusted Odds Ratio ^c	SE	Adjusted Odds Ratio ^c	SE
Mood-incongruent features (N=30)	1.2	0.97	1.4	0.71
Mood-incongruent features including patients with both grandiose and persecutory delusions (N=38)	5.7	1.27	3.8	0.90
First-rank symptoms (N=11)	20.1 ^d	1.28	4.8 ^e	0.89
Male gender (N=24)	11.7 ^f	1.16	1.1	0.69
Not first episode (N=39)	5.2	1.2	5.8 ^g	0.9

^aModified Vocational Status Index (9).^bModified Location Code Index (25).^cAdjusted simultaneously for all variables with logistic regression.^dp=0.02.^ep=0.08.^fp=0.03.^gp=0.05.

cases). For mood congruence, kappa=0.78 (SD=0.09) (p<0.0001), and for first-rank symptoms, kappa=0.70 (SD=0.12) (p<0.0001).

Outcome Assessment

Patients were evaluated 6 and 48 months after discharge, as described elsewhere (9). Briefly, three outcomes were evaluated: 1) relapse (within the follow-up period), 2) interepisode symptoms, defined as psychiatric symptoms in the absence of a full *DSM-III* affective syndrome, and 3) residential status and occupational status. Residential status and occupational status were operationally defined by using the Modified Vocational Status Index (9) and the Modified Location Code Index (25).

Relapse was documented with the use of an abridged DIS (the sections on affective and psychotic disorders) (9). The use of the DIS also permitted us to assess the stability of the index diagnoses. To establish the reliability of the diagnosis obtained at the 4-year follow-up, an investigator blind to the diagnosis independently diagnosed patients with all available documentation. The kappa statistic for the agreement on diagnoses was 0.78 (SD=0.15) (p<0.001). There were two disagreements: in one case a patient was diagnosed as having bipolar disorder by one rater and schizoaffective disorder by the other and in the second case a patient was diagnosed as having schizoaffective disorder by one rater and schizophrenia by the other.

Interepisode symptoms were assessed by using the Brief Psychiatric Rating Scale (BPRS) (26) and the Bowditch Rating Scale (27); the latter rates hallucinations, delusions, affect, and speech on a scale of 0 (not present) to 10 (so severe as to interfere with meaningful function). The interrater reliability coefficient for

the Bowditch Rating Scale and the BPRS was 0.87 (p=0.001) (9).

Statistical Analysis

For categorical outcomes, adjusted odds ratios with 95% confidence intervals were obtained for the hypothesized risk factors, controlling simultaneously for the effects of age, gender, and history of previous episodes. A logistic regression model was fitted with the computerized Statistical Analysis System (SAS) (28).

To estimate relapse risk we analyzed survival curves by using Cox proportional hazard regression models with SAS assistance (28). Hazard ratios with 95% confidence intervals were obtained, again adjusting for age, gender, and presence of previous episodes.

RESULTS

Outcome information was obtained for all 54 subjects: three (5.6%) had committed suicide, 14 (25.9%) were interviewed face to face, and 37 (68.5%) were interviewed over the telephone. We reported elsewhere (9) the high reliability of the data collected by telephone.

At the 4-year evaluation, five (9.3%) of the 54 subjects had shifted diagnosis—four to schizoaffective disorder and one to schizophrenia. Twenty-seven (50%) were receiving antipsychotic drugs. The presence of mood-incongruent psychotic features during the index episode was associated with use of antipsychotic drugs at 4 years (adjusted odds ratio=5.9, confidence interval=1.5–24.2, p=0.01) after controlling for age, sex, and presence of previous episodes. No significant associations were found between type of psychotic feature during the index episode and sociodemographic variables, presence of previous episodes, or shift in diagnosis at 4 years.

Psychosocial Outcome

Logistic regression was used to predict psychosocial outcome at 4 years (table 2). Presence of first-rank symptoms and male gender predicted poor residential status after controlling for presence of mood-incongruent features, age, and presence of previous episodes (table 2). Presence of first-rank symptoms after controlling for the same variables almost reached statistical significance for the prediction of poor vocational status at 4 years (table 2). Mean age at index episode (30 years, SD=9.4) did not predict residential status (beta coefficient=-0.02, SE=0.04) or occupational status (beta coefficient=0.03, SE=0.04) at 4 years. No predictors were identified for poor outcome at the 6-month follow-up.

Relapse

Forty-one (75.9%) of the 54 patients suffered at least one episode of illness during the 4-year follow-up period.

In 17 (31.5%) of the 54 patients the first episode of relapse was depression and in 24 (44.4%) it was mania.

Mood-incongruent psychotic features predicted a shorter time in remission (hazard ratio=2.6, 95% confidence interval=1.2-5.5, $p=0.01$) after controlling for gender, age, and presence or absence of previous episodes. The median time in remission for patients with mood-incongruent psychotic mania was about 8 months, compared with 33 months for the patients with mood-congruent psychotic mania ($\chi^2=6.01$, $df=4$, $p=0.01$) (figure 1). When we classified the patients with predominantly grandiose and persecutory delusions as having mood-incongruent psychotic mania, we found no difference in risk of relapse between the mood-congruent and the mood-incongruent groups.

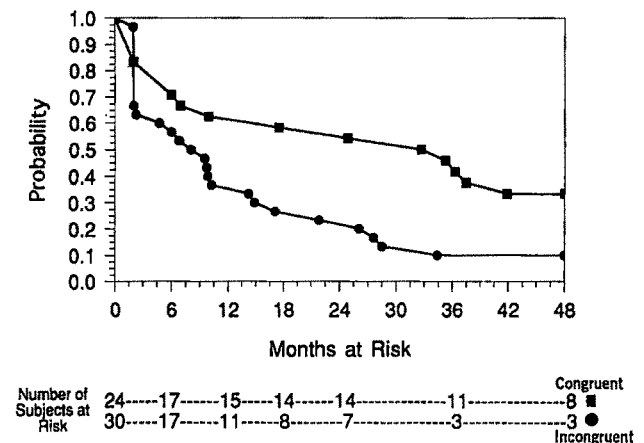
No predictors were identified for the presence of interepisode symptoms at 6 or 48 months.

DISCUSSION

It appears that the differentiation of mood-congruent and mood-incongruent psychotic features in mania has prognostic validity, adding support to this proposed distinction in *DSM-III-R*. Our findings indicate that presence of mood-incongruent psychotic features represents a risk factor for episode relapse in bipolar disorder, especially during the first year after recovery from an index episode of mania. Therefore, contrary to some previous reports (2, 3, 8, 29) but in agreement with others (5-7, 17, 19), the characteristics of psychotic symptoms during an index manic episode may have value in predicting the later course of bipolar illness. Mood incongruence also has been found to predict poorer outcome in major depression (11). The value of identifying first-rank symptoms in mania or depression has been questioned (29), and low reliability in its assessment has been suggested (30). However, we found good reliability in the identification of both first-rank symptoms and mood congruence. In our group of patients, presence of first-rank symptoms predicted poor psychosocial outcome at 4 years, suggesting the utility of their assessment in manic patients.

The identification of mood congruence as a predictor of outcome in mania may speak to a gradation of vulnerability in which mania without psychotic features has the best prognosis (9, 10), mania with mood-incongruent psychotic features has the worst prognosis, and mood-congruent psychotic features occupy a middle position regarding future risk. Thus, the present report supports a "severity continuum" hypothesis, as suggested by others (19, 31, 32). Furthermore, a recent 5-year follow-up study conducted by Coryell et al. (33) found that patients with schizoaffective mania had worse outcomes than patients with psychotic mania. Adhering to a continuum hypothesis, it would follow that schizoaffective mania would then be at the extreme of a severity scale. Furthermore, close to 10% of our study group had a change in diagnosis at the 4-year follow-up, which is similar to rates reported by other in-

FIGURE 1. Cumulative Probability of Remaining in Remission Over 48 Months for 54 Patients With Mood-Congruent and Mood-Incongruent Psychotic Mania



vestigators (34, 35). As recently discussed by Taylor (36), the boundaries of affective disorders, schizoaffective disorders, and schizophrenia need to be further investigated.

The identification of different courses and outcomes in a presumably single disorder represents an external validator of a nosological distinction (37). The present report suggests that manic episodes with mood-incongruent psychotic features may represent a severe presentation of bipolar disorder.

The issue of classifying psychotic mania as mood congruent or mood incongruent needs further clarification in the *DSM* system. Currently, there are no clear guidelines on how to classify an episode if both types of psychotic features are present. This differentiation is particularly relevant when grandiose and persecutory delusions are both present because they are the most common type of delusions experienced by manic patients (13). Our findings suggest that if both types of delusions are present and the episode is classified depending on which type is predominant, the two groups will differ in terms of risk to relapse. On the other hand, when we used the mere presence of persecutory delusions to classify our patients' episodes as mood incongruent there were no differences in outcome. Another option is to have a category defined as presence of both mood-congruent and mood-incongruent psychotic features. Only a few ($N=12$) of our subjects had both types of features, so we could not conduct further analysis of this possibility. The utility of such a category needs further validation.

Generalizations from the present findings should be made cautiously. These results may apply only to patients with bipolar disorder who recovered from an index manic episode that required hospitalization. Therefore, our subjects may represent less severely ill patients with bipolar disorder because they recovered from the index manic episode. On the other hand, a higher proportion of our patients than of other reported subjects

(13) had mood-incongruent features, which may suggest that our patients were more severely ill. In addition, due to the uncontrolled nature of treatment, no definite conclusions can be drawn as to the impact of treatment interventions on outcome or their interaction with mood-congruent or mood-incongruent psychotic features.

By identifying a significant association between the 4-year course of mania and mood congruence of psychotic features, the present report supports the validity of this nosological distinction, recently advocated by Kendler (19). It also highlights the importance of phenomenological and longitudinal assessment of patients with bipolar disorder. To further investigate the issue of stability of affective and psychotic disorders, prospective follow-up studies need to be conducted with diagnostic assessments at first episode and across longer periods of time. Finally, clinicians need to be aware of a possibly unfavorable outcome in manic patients with mood-incongruent psychotic features.

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Psychotic Symptoms and Suicidal Behavior in Hospitalized Children

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Association of psychotic symptoms with suicidal behavior was studied in 90 hospitalized pre-pubertal children. Children with psychotic symptoms were more likely to have threatened or attempted suicide. The association of visual hallucinations with suicidal behavior was stronger than that of auditory hallucinations or psychotic ideation. The authors speculate that psychosis in general and visual hallucinations especially may be indicators of suicide risk among children.
(Am J Psychiatry 1992; 149:1585-1586)

Psychotic symptoms, including auditory, visual, and tactile hallucinations and delusional ideas, are commonly reported by children with major depression (1, 2). Depression is clearly established as a major risk factor for suicide in childhood, and there is evidence for a relationship of psychosis to severity of depression as well as to particular suicide-encouraging content in the hallucinations of depressed children (3). Shaffer et al. (4) observed a high rate of suicide among adolescents suffering from psychosis. Taken together, these findings suggest a need to look for associations of psychotic symptoms with suicidal behavior in younger children as well.

Suicidal behavior is a common reason for hospitalizing children in psychiatric units, so we used data from a hospital study group to test the following hypotheses: 1) children with psychotic symptoms are more likely to have engaged in suicidal behavior than children without psychotic symptoms, and 2) among psychotic symptoms, auditory hallucinations will be most highly correlated with suicidal behavior.

METHOD

One hundred children admitted consecutively to a children's psychiatric unit were given the Diagnostic In-

terview for Children and Adolescents, the methodology for which was described previously (5). The interview was administered by trained medical students and scored by the first author using *DSM-III-R* criteria. The suicide items of the Diagnostic Interview for Children and Adolescents and the recorded presence or absence of suicidal statements or attempts in the admission histories were used to determine suicidal behavior. Psychotic symptoms from the relevant section of the Diagnostic Interview for Children and Adolescents were scored as present or absent.

Of the 100 consecutively admitted children, five were discharged within 48 hours and therefore were not given the diagnostic interview, and five other children were excluded from the study because of incomplete or questionable responses in the interview. The 90 study subjects included 64 boys and 26 girls; 80% (N=72) were white and 20% (N=18) were black. Formal socioeconomic status ratings are not available, but 48 children (53.3%) were on public assistance. The children's ages ranged from 6 to 12 years (mean=9.9 years, SD=1.9). The mean IQ according to the WISC-R was 92 (SD=17).

RESULTS

Sixty-two children had more than one diagnosis according to the Diagnostic Interview for Children and Adolescents; the mean number of diagnoses for the group was 2.8 (SD=1.6). Seventeen children had major depression, and another 18 had more chronic depressive symptoms but did not fulfill the criteria for major

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TABLE 1. Psychotic Symptoms in Suicidal and Nonsuicidal Hospitalized Children

Psychotic Symptoms	Suicidal Children (N=39)	Non-suicidal Children (N=51)	Analysis		Odds Ratio
			χ^2 (df=1) ^a	p	
Visual hallucinations	5	1	13.2	<0.01	30.0
Auditory hallucinations	7	10	<1.0	n.s.	0.9
Any psychotic symptom	27	22	5.1	<0.05	3.2
Persecutory or referential ideas	7	17	<1.0	n.s.	0.4
Other psychotic ideas	7	8	<1.0	n.s.	1.2

^aWith Yates's correction.

depression (they were clinically dysthymic, but the interview did not, until the more recent revision, explicitly address dysthymia). Thirty-nine children had only a behavior disorder (conduct disorder, oppositional defiant disorder, or attention deficit hyperactivity disorder). Other diagnosed emotional disorders, many in children who also had depression, included separation anxiety disorder (N=13) and overanxious disorder (N=16).

Seventeen children reported auditory hallucinations other than hearing their names called; all involved distinct voices either making derogatory comments or commanding them to harm themselves or others or engage in other forbidden acts. Six children, all boys, reported visual hallucinations, all of them of dead relatives. Twenty-four children acknowledged ideas of reference or persecution, and 15 reported thought broadcasting, thought insertion, mind reading, or other unusual thought experiences. In only eight cases were these judged to be delusional in proportion, and these eight children also had hallucinations. All of the children with hallucinations had one of the depressive diagnoses. Fifteen of the children who reported psychotic symptoms other than hallucinations reported at least some depressive symptoms.

Thirty-nine patients reported suicidal ideation. All of them had also made either suicidal statements/threats (N=22) or suicide attempts with or without threats (N=17). All 17 patients with major depression were in the group exhibiting suicidal behavior, as were 11 of the 18 with chronic depression.

The association of major depression with suicidal behavior was highly significant ($\chi^2=24.6$, df=1, $p<0.001$). Overall, children with depressive diagnoses were 16 times as likely to have threatened or attempted suicide as children without depressive disorder.

Five children who reported visual hallucinations of dead relatives had made multiple suicide attempts. Persecutory or referential ideas were reported by six who threatened suicide but only one who attempted suicide. Table 1 provides an overall comparison of psychotic symptoms in the suicidal (attempters and threateners) and nonsuicidal children interviewed.

The children who had attempted suicide differed in some respects from those who had threatened suicide. All of the attempters but only half of the threateners had a depressive disorder, and six of the threateners but only one attempter had persecutory or referential ideas.

DISCUSSION

Our first hypothesis is supported by these data: children with psychotic symptoms were three times as likely as nonpsychotic children to show suicidal behavior. The hypothesized specific risk associated with auditory hallucinations was not observed: children with visual hallucinations were more suicidal. Although the number is small, this finding is striking and deserves further exploration in relation to reunion fantasies, children's views of death, and the relation between grief and depression in youth.

Other findings that need further study include the possible association of persecutory ideas with suicide threats but not suicide attempts and the apparent lack of association of suicidal behavior with auditory hallucinations. Ideally, all of these associations will generate hypotheses for future study of both disturbed populations like ours and samples representative of broader populations, with some rating of suicidal behaviors as more and less serious both psychiatrically and medically.

Although the study of suicidal behavior among children and adolescents has recently accelerated, our current knowledge of risk factors for suicide among youngsters is extremely limited. We know that suicide threats and attempts are usually present in the histories of young people who commit suicide, and we know that depressive disorders are associated with suicidal statements and suicide attempts (3, 4). Our results indicate that in prepubertal children, psychotic symptoms in general and visual hallucinations of dead relatives in particular may increase the risk of suicidal behavior. We strongly recommend that these symptoms be inquired about as part of clinical assessment for suicide risk.

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Amelioration of Mitral Valve Prolapse After Treatment for Panic Disorder

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Twenty panic disorder patients with mitral valve prolapse showed amelioration of prolapse on repeat echocardiogram after treatment for panic disorder. This effect was significant when compared to repeat echocardiograms in eight psychiatrically normal control subjects with mitral valve prolapse.

(Am J Psychiatry 1992; 149:1587-1588)

The association of panic disorder and mitral valve prolapse is controversial. Studies have reported a greater than average prevalence of mitral valve prolapse in patients with panic disorder, although others have not confirmed this association (1, 2). Gorman et al. (1) reported that the majority of patients with panic disorder and mitral valve prolapse suffer from mild prolapse that is hemodynamically and clinically insignificant. This may be missed by overly stringent criteria and may account for discrepancies among studies.

Investigators have argued that mitral valve prolapse initiates panic disorder (3), that mitral valve prolapse and panic disorder are associated by mere chance (4), and that panic disorder causes mitral valve prolapse (5). In order to test the last hypothesis, we report on patients with panic disorder and mitral valve prolapse who underwent repeat echocardiograms after treatment for panic disorder.

METHOD

Subjects

Twenty subjects who met *DSM-III* criteria for panic disorder with or without agoraphobia and who showed

echocardiographic evidence of mitral valve prolapse were studied. The mean age of these subjects was 37.3 years ($SD=7.8$); there were five men and 15 women. Eight psychiatrically normal control subjects who showed incidental echocardiographic evidence of mitral valve prolapse were also included. Their mean age was 29.0 years ($SD=4.6$); there were two men and six women. Informed consent was obtained after the procedure was explained.

Procedure

All echocardiograms were performed by M-mode and two-dimensional techniques, with patients in the lateral decubitus position, and were read by the same cardiologist (D.L.K.). Mitral valve prolapse was diagnosed on two-dimensional imaging when posterior movement of either or both mitral valve leaflets relative to the annulus was observed during systole. On the M-mode tracing, mitral valve prolapse was manifested as an abrupt posterior change of direction of the mitral echo during systole; the normal echo usually inscribes a straight line. Severity of the prolapse was rated by M-mode as 1) no prolapse, 2) borderline prolapse: 2 mm or less, 3) mild prolapse: 3-4 mm, 4) moderate prolapse: 5-7 mm, and 4) severe prolapse: 8-10 mm.

Patients were then treated in an open fashion. Seven received only benzodiazepines, three received tricyclic antidepressants, and four received both. One patient received a tricyclic antidepressant, a benzodiazepine, and behavioral therapy, one a tricyclic antidepressant and lithium, and one a tricyclic antidepressant and behavioral therapy. One received a tricyclic antidepressant/monoamine oxidase inhibitor (MAOI) combination, and one received an MAOI with a benzodiazepine. Information on treatment and clinical status of one patient was not available. All patients showed some clinical improvement; 12 were evaluated as panic free and

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seven as having a reduction of frequency and/or intensity of panic symptoms at the time of the second echocardiogram.

After a mean treatment period of 27.8 months ($SD=21.6$), the subjects underwent a repeat echocardiogram. Repeat echocardiograms were performed on the control subjects after a mean of 13.3 months ($SD=2.3$).

Data Analysis

The first analysis compared the ratio of patients who did not have evidence of mitral valve prolapse on repeat echocardiogram to those whose status did not change versus the same ratio in control subjects. We initially used a displacement cutoff point of 2 mm or greater to define mitral valve prolapse. We then repeated the analysis using a 3-mm cutoff, which has been viewed by cardiologists as the preferable standard for diagnosing prolapse (6). We also performed a Student's *t* test comparing the mean change in degree of prolapse from first to second echocardiogram between patients and control subjects. In a number of instances, the echocardiographer noted only the severity of prolapse on the report, not the millimeters of displacement. In those cases the following conversion was used: borderline—2 mm, mild—3.5 mm, moderate—6 mm, severe—9 mm.

RESULTS

The control group was younger than the patients ($t=2.8$, $df=26$, $p<0.005$). Baseline differences in degree of prolapse or sex differences between groups were not detected. The interval between echocardiograms was longer for patients than for control subjects ($t=1.9$, $df=26$, $p<0.04$). When the 2-mm cutoff point was used, 12 of 20 patients who originally had mitral valve prolapse were categorized as not having it. Of eight control subjects, two were categorized as not having mitral valve prolapse on repeat echocardiogram (from borderline to no mitral valve prolapse in both instances) (*n.s.*). When the analysis was repeated with the 3-mm cutoff point, nine of 15 patients were categorized as having no mitral valve prolapse after treatment for panic disorder, compared to none of six control subjects (Yates's $\chi^2=4.1$, $df=1$, $p<0.05$). Five patients and two control subjects with borderline prolapse on the first echocardiogram were excluded when the 3-mm cutoff was used. When the change in degree of prolapse between echocardiograms was compared, the patients showed a mean decrease in prolapse of 1.8 mm ($SD=1.8$), compared to a slight increase in prolapse in the control subjects (mean=0.1 mm, $SD=2.7$) ($t=2.2$, $df=26$, $p<0.02$).

DISCUSSION

The findings of this preliminary study suggest that mitral valve prolapse associated with panic disorder may be a consequence of the disorder itself. Although the analysis that used the 2-mm cutoff did not show a significant mitral valve prolapse conversion rate, when the more conservative 3-mm cutoff was used, the conversion rate became statistically significant. Further, the *t* test analysis, which did not use a specific cutoff point, showed an overall reduction in degree of prolapse in patients compared to control subjects. These findings should be qualified by certain methodological limitations, which include that the patient group were significantly older and had significantly longer intervals between echocardiograms than control subjects. Future replicative studies should carefully control for such factors, since they may have confounded the results of the present study.

The prolapse associated with panic disorder may result from autonomic overdrive, leading to temporary deformation in the mitral valve or desynchrony in ventricular contraction (7). Since patients received a number of treatments, including nonpharmacological ones, it is likely, but not yet proven, that the resolution of the prolapse was not due to a direct pharmacological effect but rather due to a general reduction in panic symptoms. A possible mechanism for amelioration of prolapse may result from an attenuation of autonomic overdrive, an effect of antipanic treatment (8).

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Hyperventilation-Induced Cerebral Ischemia in Panic Disorder and Effect of Nimodipine

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Basilar artery blood flow was measured by transcranial Doppler ultrasonography before and during hyperventilation in nine patients with panic disorder and nine normal comparison subjects. The hyperventilation-induced decrease in basilar artery blood flow was significantly greater in patients with panic attacks than in comparison subjects. Two patients with decreases in basilar flow greater than 80% were successfully treated with nimodipine, a centrally active calcium channel blocker.

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Although hyperventilation and hypersensitivity to changes in the partial pressure of carbon dioxide in arterial blood (arterial PCO_2) have been proposed as mechanisms involved in the symptoms of panic attacks, the exact role, if any, of hyperventilation has remained obscure (1, 2). This study was designed to test the hypothesis that panic disorder is associated with greater sensitivity of cerebral arteries to changes in arterial PCO_2 by measuring basilar artery blood flow with transcranial Doppler ultrasonography before and during hyperventilation. During the study, two patients with panic disorder were identified who had extraordinary reductions in basilar artery flow velocity during hyperventilation associated with substantial neurological symptoms. These two patients were treated with nimodipine, a centrally active calcium channel blocker that selectively dilates cerebral arterioles and limits calcium influx in CNS neurons (3). Both patients had normalization of basilar artery flow velocities and pulsatility during hyperventilation and marked improvement in symptoms in response to nimodipine.

METHOD

Nine patients meeting *DSM-III-R* criteria for panic disorder and nine healthy comparison subjects of similar age and sex were studied by transcranial Doppler ultrasonography before and during hyperventilation by using a Biosound Genesis II vascular ultrasound unit with transcranial Doppler capabilities (4). Two of the

patients with panic disorder were taking tricyclic antidepressants and the rest were drug free. All subjects gave informed consent. The basilar artery was insonated through the foramen magnum at a depth of 80–85 mm. Results are expressed as the mean flow velocity in centimeters per second and as the pulsatility index. The pulsatility index is equal to the peak systolic velocity minus the final diastolic velocity divided by the mean velocity. Generally, an increase in pulsatility index is an indication of increased vascular resistance distal to the segment of artery sampled by ultrasound. Hyperventilation was performed until a stable, minimum basilar flow velocity was achieved. This usually occurred within 60–90 seconds. Differences between patients and comparison subjects were analyzed by using a group *t* test or a two-factor analysis of variance with repeated measures as appropriate.

RESULTS

There were no significant differences between the nine patients with panic disorder and the nine comparison subjects in age (mean=40.1 years, SD=9.6, versus mean=38.4, SD=9.6, respectively), in baseline mean basilar artery flow velocity (mean flow velocity) (38.1 cm/sec, SD=12.5, versus mean=40.4 cm/sec, SD=6.0), or in baseline pulsatility index (mean=0.85, SD=0.16, versus mean=0.85, SD=0.12). As shown in figure 1, hyperventilation produced a significantly greater reduction in basilar artery flow velocity in patients with panic disorder than in comparison subjects (62% versus 36%) and a much greater increase in the pulsatility index.

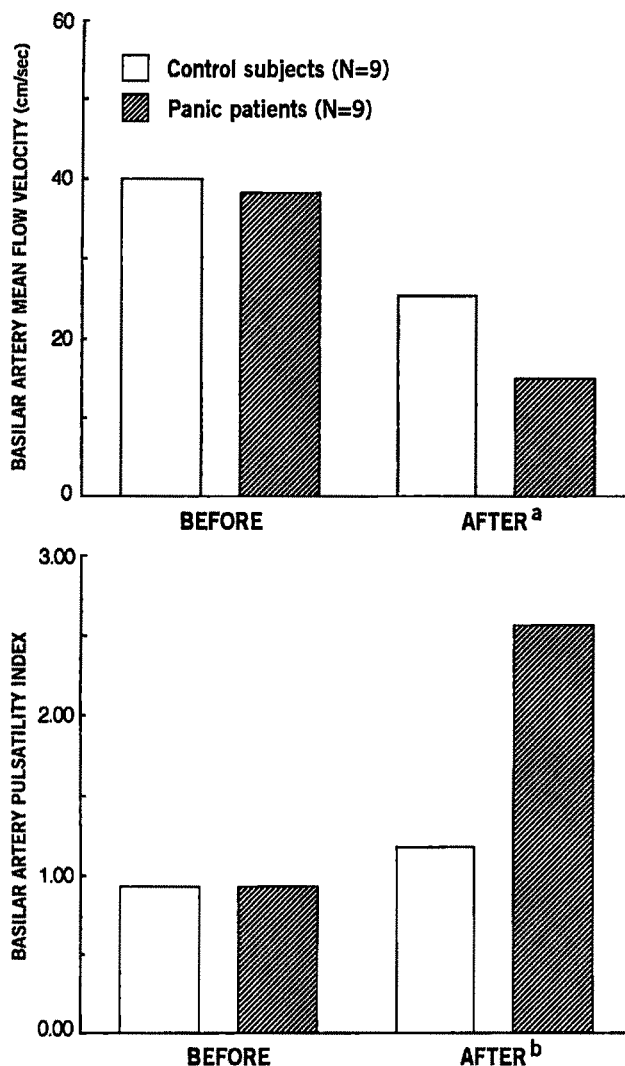
Two patients were found to have a greater than 80% reduction in basilar artery mean flow velocity during hyperventilation. The histories of these patients are presented here. Each was treated with 30 mg of nimodipine orally three times per day. Repeat transcranial

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Nimodipine was supplied by Miles Laboratories.

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FIGURE 1. Effects of Hyperventilation on Basilar Artery Mean Flow Velocity and Pulsatility Index in Patients With Panic Disorder and Normal Comparison Subjects



^aMain effect: $F=3.1$, $df=1, 16$, $p<0.10$; interaction: $F=8.0$, $p<0.01$.

^bMain effect: $F=5.2$, $df=1, 16$, $p<0.05$; interaction: $F=7.2$, $p<0.02$.

nial Doppler studies were performed after 4 weeks of treatment.

Case 1. This 44-year-old man began to have unexplained syncope in adolescence. The spells resolved when he was a young adult but returned in conjunction with a severe anxiety disorder about 5 years ago. They reached a peak frequency of 5–7 spells per day of syncope or pre-syncope, each preceded by a sense of impending doom, vertigo, tachycardia, and diaphoresis. He underwent extensive evaluations, including cardiac monitoring, cardiac catheterization, carotid duplex ultrasonography, magnetic resonance imaging (MRI) studies of the head, and three EEGs. The results of all of these tests were normal. His spells had been treated unsuccessfully with a variety of medications including diazepam, doxepin, phenytoin, divalproex sodium, primidone, verapamil, clonidine, propranolol, and acetazolamide. Other history of note included premature birth (32-week gestation), classic migraine head-

aches at least once per week, chronic daily headaches, and hypertension. Results of the neurological examination were entirely normal.

Case 2. This 37-year-old man had a 10-year history of panic attacks that occurred 1–3 times per day. During this same period he experienced recurrent paresthesias, primarily in the left leg but also in the right leg as well as in the hands and neck. Extensive evaluations over the last 10 years have included multiple nerve conduction studies and EMGs, somatosensory evoked potentials, MRI studies of the brain and entire spine, a spinal fluid examination, metabolic testing for a variety of muscle diseases, a muscle biopsy, and consultations with at least five neurologists. Results of all tests have been normal. His past medical history was otherwise unremarkable, and results of the neurological examination were normal. He was taking no medications.

Both of these patients had low baseline basilar mean flow velocity (table 1); their baseline values were lower than those of any other patients or comparison subjects. Both had a greater than 80% decrease in flow and a very large increase in pulsatility during hyperventilation. After 4 weeks of treatment with nimodipine, the basilar mean flow velocity and pulsatility index responses to hyperventilation of both patients had returned to normal. Patient 1 had complete relief from his syncopal spells within 2 days of the onset of treatment. After 4 weeks of treatment, he decided to stop taking nimodipine because he felt that his chronic daily headaches were worse. However, his spells returned and he insisted on taking nimodipine again. Patient 2 also noted a marked decrease in the frequency and severity of his panic attacks as well as in his long-standing paresthesias.

An additional patient with more typical cerebral vasoreactivity (50% reduction in basilar flow velocity after hyperventilation) was treated with nimodipine. For this patient, nimodipine caused absolutely no change in either baseline or posthyperventilation flow velocity, pulsatility, or the frequency, quality, or severity of her panic attacks.

DISCUSSION

The nine patients with panic disorder as a group tended to have an exaggerated reduction in basilar artery blood flow during hyperventilation compared with comparison subjects. Not all of the patients in this study had greater responses than comparison subjects, but those who did tended to be the ones who developed neurological symptoms during their attacks. This relative cerebral ischemia during hyperventilation is probably not the fundamental cause of panic attacks but, rather, may be the mechanism responsible for some of the associated symptoms that reinforce the sense of panic.

The effect of nimodipine in normalizing blood flow responses to hyperventilation and ameliorating neurological symptoms in two patients was striking. Nimodipine readily crosses the blood-brain barrier and

TABLE 1. Effect of Nimodipine on Basilar Artery Flow Responses to Hyperventilation in Two Patients With Panic Disorder

Condition and Patient	Mean Flow Velocity			Pulsatility Index		
	Velocity (cm/sec)		Change (%)	Index		Change (%)
	Baseline	After Hyperventilation		Baseline	After Hyperventilation	
Before Nimodipine						
Patient 1	29	5	-83	1.03	5.60	443
Patient 2	26	5	-81	1.04	4.80	361
After Nimodipine						
Patient 1	34	23	-32	0.94	1.70	80
Patient 2	42	21	-50	0.93	2.38	156

acts on cerebral neurons to limit influx of calcium ions. This is the presumed mechanism by which nimodipine lessens ischemic damage after subarachnoid hemorrhage and stroke (5) and slows the progression of some organic dementias (6). The possibility that nimodipine is working on the symptoms of panic attacks by direct effects on CNS neurons, therefore, cannot be excluded. However, since nimodipine is also a potent and selective dilator of cerebral arteries, a more important site of action in panic disorder is likely the smooth muscle of cerebral arteries. Verapamil, a nonselective calcium channel antagonist that does not cross the blood-brain barrier, has previously been shown to have a modest beneficial effect in panic disorder (7), supporting a vascular site of action for these agents.

The two patients who responded to nimodipine in this study had extraordinary responses to hyperventilation and consequently had associated neurological symptoms that were more remarkable than most patients with panic disorder. Although the responses of these two patients to nimodipine were dramatic both subjectively and objectively, a more typical patient did not respond to nimodipine, suggesting that only a sub-

set of patients with panic disorder and severe hyperventilation-induced ischemia might benefit from nimodipine or other centrally active calcium channel antagonists.

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Accumulation of Fluoxetine and Norfluoxetine in Human Brain During Therapeutic Administration

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In vivo ^{19}F nuclear magnetic resonance spectroscopy was used to measure the brain concentration of fluoxetine and norfluoxetine in five patients with obsessive-compulsive disorder and three with major depression. The mean brain:plasma ratio of the parent drug plus the metabolite was significantly elevated to 2.6 ($SD=1.0$) (95% confidence interval=1.9–3.3). This accumulation may have implications for understanding both the therapeutic and the toxic effects of fluoxetine.

(Am J Psychiatry 1992; 149:1592–1594)

The potential that in vivo nuclear magnetic resonance spectroscopy (MRS) holds for research in psychiatry has been the subject of recent reviews (1, 2). From a psychopharmacological perspective, MRS offers a means of noninvasively measuring the brain levels of those drugs which are MRS-visible. These agents include lithium and psychotropic medications that contain fluorine. To date, in vivo brain resonances have been detected in human subjects taking lithium, trifluoperazine, fluphenazine, and fluoxetine (3–5). The rationale for this work lies in the hypothesis that a knowledge of the brain levels of these drugs may contribute to an understanding of both their therapeutic and their toxic effects. Unfortunately, except for lithium, it has been difficult to quantitate brain drug levels or to correlate these values with corresponding plasma levels. Additionally, reports of spectra derived from subjects taking fluorinated psychotropic agents have generally consisted of data from a single subject taking unusually high doses of medica-

tion (e.g., 120 mg/day of trifluoperazine [4] and 350 mg/17 days of fluphenazine decanoate [5]).

Fluoxetine is a serotonin reuptake inhibitor that has been used successfully to treat major depression, obsessive-compulsive disorder, and bulimia. Both fluoxetine and its long-lived active metabolite, norfluoxetine, are trifluorinated. We used ^{19}F MRS to measure the brain level of fluoxetine plus norfluoxetine in eight patients with major depression or obsessive-compulsive disorder. In each patient, the brain level of fluoxetine plus norfluoxetine was several times higher than the plasma level.

METHOD

Our experimental protocol was approved by the human subjects committee of our hospital, and informed consent was obtained from each subject before his or her participation. Eight subjects took part in the study. All had been taking fluoxetine for a minimum of 3 months (mean=13 months, $SD=6$), and none had a dose change within 4 weeks of the study. Four subjects were taking 60 mg/day, three were taking 80 mg/day, and one was taking 100 mg/day of fluoxetine. Five patients had a *DSM-III-R* diagnosis of obsessive-compulsive disorder, and three had a *DSM-III-R* diagnosis of major depression. The patients' mean age was 34 years ($SD=8$); four were men and four were women. Four patients were taking at least one other medication (two were taking clonazepam, one was taking lithium, and one was taking methylphenidate). The clinician of each patient felt that the patient had improved markedly in response to fluoxetine.

A commercially available 1.5 Tesla whole body imager was used to collect in vivo spectra with a home-

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Fluoxetine hydrochloride and norfluoxetine maleate were supplied by the Eli Lilly Co.

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built, 21-cm-inner-diameter, cylindrical head coil tuned to 60.1 MHz. Each patient was positioned so that only the upper half of his or her head (to the tip of the nose) was within the sensitive volume of the coil, and the magnet was shimmed on the water proton resonance to within 20–30 Hz over the sampled volume. A nonselective 90° pulse was used with a repetition time (TR) of 2 seconds, and 300 acquisitions were averaged over a 10-minute period in collecting ^{19}F spectra. For three of the eight patients, two independent measurements separated by a period of 30 minutes were made to evaluate the reproducibility of the technique.

Brain concentrations were calculated by comparison of the integrated intensity of the in vivo resonance with that arising from a 1450 cm³ cylindrical phantom containing 8.8 mg/liter of fluoxetine in 140 mM of sodium chloride (3, 4). The intensity of the phantom resonance was measured immediately after completion of the clinical study. The in vivo resonance was assumed to be derived primarily from the brain. Brain volumes for each subject were calculated from T₁-weighted axial images by using a volumetric image analysis program developed in-house; the estimated accuracy of this program for objects the size of a whole brain is plus or minus 5% at one standard deviation (unpublished data). The average total brain volume (cerebrum, cerebellum, and brain stem to the base of the pons, including ventricles) was 1360 cm³ (SD=170) for these eight subjects. The single observed resonance was thought to arise predominantly from both fluoxetine and norfluoxetine; pure samples of each had identical chemical shifts at high field (376 MHz). With TR=2 seconds, the phantom resonance was 73% of the fully relaxed value while brain resonances did not change consistently with TR=1, TR=2, or TR=4 seconds in two subjects.

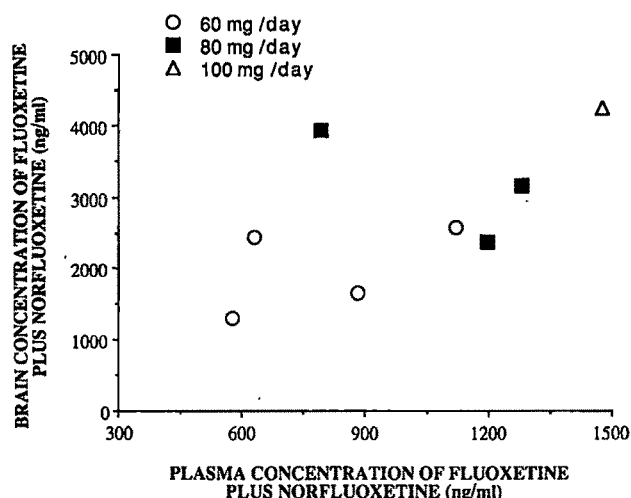
Blood samples were collected at the time spectroscopy was performed. Plasma levels were measured by a commercial laboratory using gas chromatography with electron capture detection; this assay is said to be reproducible to within 13% at one standard deviation for both fluoxetine and norfluoxetine given the range of values obtained in this study. The concentration of fluoxetine in the phantom was determined by using high performance liquid chromatography with a photodiode array detector. This assay was performed in-house to correct for possible artifacts arising from the lack of plasma in the sample; duplicate analysis yielded concentrations of 8.7 and 8.9 mg/liter of fluoxetine, respectively.

RESULTS

Figure 1 outlines our results. Calculated brain concentrations of fluoxetine and norfluoxetine were 2.6 times higher than corresponding plasma levels. The difference between brain and plasma levels was statistically significant when a two-tailed paired *t* test was applied (*t*=5.59, *df*=7, *p*<0.0008).

Daily dose correlated more closely than plasma level

FIGURE 1. Plasma Versus Brain Drug Concentrations of Fluoxetine Plus Norfluoxetine in Eight Patients Receiving Different Doses of Fluoxetine^a



^aFor the correlation between plasma and brain drug level, *r*=0.58, *df*=7; for the correlation between daily dose and brain level, *r*=0.82, *df*=7. Mean ratio of brain to plasma drug level=2.6 (SD=1.0) (95% confidence interval=1.9–3.3).

with calculated brain levels (figure 1). The poor correlation between plasma and brain levels was disproportionately affected by values obtained from one of the eight patients whose brain level was 4.9 times higher than her plasma level. When data from this patient are excluded, the correlation coefficient between plasma and brain levels improved (*r*=0.82, *df*=6). It is unclear why the data from this one patient are so divergent; unfortunately, she refused to undergo repeat MRS or to allow a repeat determination of her plasma drug levels.

For the three patients who underwent repeated MRS measurement, duplicate values of brain concentration varied by 2%, 4%, and 9%.

DISCUSSION

Our results are limited by both clinical and technical factors. At a clinical level, we were concerned with being able to maximize the reproducibility of our brain measurement. Therefore, we sought to study individuals taking a range of relatively high doses of fluoxetine, which resulted in greater intensity of the detected resonance and allowed us to make measurements that were reproducible to within about 10%. However, in so doing, we ended up studying a clinically heterogeneous population and thus are unable to comment on whether the uptake of fluoxetine varies with diagnosis.

Technically, our results are limited by at least three factors. First, the low sensitivity of the MRS technique requires that data must be collected over an extended period of time (approximately 10 minutes). To increase the accuracy of our measurement by a factor of two with addi-

tional signal averaging, the patient would have to remain in the magnet for approximately 40 minutes.

Second, our results are influenced by the fact that spectra were collected without the use of a technique for spatial localization (1, 2). Thus, the assumption that the observed signal derives entirely from the brain neglects the contributions from the ventricular CSF and the surrounding extracranial tissues but assumes that the blood within the cerebral vasculature contributes to the observed resonance. Fortunately, the CSF in man is known to contain very low concentrations of both fluoxetine and norfluoxetine (6). In addition, there is relatively little extracranial soft tissue on the upper half of the head (the only region from which the signal was collected given the placement of our coil), so these contributions should produce a relatively minor elevation of the calculated brain level. On the other hand, since the calculated brain concentration of fluoxetine and norfluoxetine is higher than the corresponding plasma concentration, including the cerebral vasculature within the brain volume would tend to lower the calculated brain level slightly.

A third factor that affects our results is the assumption that the observed resonance is derived solely from fluoxetine and its long-lived active metabolite, norfluoxetine. In fact, other inactive metabolites that contain fluorine may also contribute to this resonance. There is relatively little published information on the tissue distribution of fluoxetine and its metabolites. However, in the pregnant rat, fluoxetine and norfluoxetine account for 47%–93% of the radioactive material recovered from maternal tissues in the 24 hours following a single injection of ^{14}C -labeled fluoxetine (7). After multiple doses, it is likely that fluoxetine and norfluoxetine, being both nonpolar and long-lived in comparison with their inactive metabolites, would be present at an even greater relative proportion.

Despite the limitations noted, our results are consistent with data derived from animal experiments. In the rat, brain concentrations of fluoxetine and norfluoxetine are several times higher than plasma concentrations following the administration of a single dose of fluoxetine (8). We are not aware of any published data on the concentration of fluoxetine or norfluoxetine in animal brain after chronic drug administration. How-

ever, accumulations of the tricyclic antidepressants clomipramine, imipramine, desipramine, and protriptyline are all roughly five to 20 times higher than plasma levels after chronic administration to rats (9). This is generally ascribed to high lipid and protein binding as well as to the synaptosomal concentration of these protonated basic drugs (10).

Although fluoxetine is thought to work on the basis of its serotonin reuptake inhibition, it may be that its apparent accumulation *in vivo* also contributes to both its therapeutic and its toxic properties. Further work will be needed to confirm these preliminary findings and to assess their significance.

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Severity of Cocaine Dependence as a Predictor of Relapse to Cocaine Use

Roger D. Weiss, M.D., Margaret L. Griffin, Ph.D., and Cathryn Hufford, B.A.

The severity of cocaine dependence of 39 hospitalized patients was assessed by administering the Structured Clinical Interview for DSM-III-R. No significant relationship was found between severity of cocaine dependence and cocaine use at 3-month follow-up. These findings suggest that severity of cocaine dependence may be a poor predictor of relapse to cocaine use. (Am J Psychiatry 1992; 149:1595-1596)

The concept of the dependence syndrome, initially proposed to describe clinical features of alcoholism (1), has been expanded to include patients dependent on other drugs (2; *DSM-III-R*). A central tenet of the dependence syndrome concept is that clinical characteristics occur along a continuum of graded levels of severity (3). Thus, *DSM-III-R* criteria for psychoactive substance dependence include three categories of severity: mild, moderate, and severe. This classification scheme has two limitations, however. First, the boundaries between these categories of severity have not been clearly delineated. Second, although empirical studies have suggested that severity of alcohol dependence is a relatively good predictor of clinical outcome (4, 5), there has been little analogous research on drug dependence. Indeed, Babor et al. (5) found severity of dependence to be a good predictor of outcome in alcoholics but not in opioid addicts. Since we are aware of no studies of this subject in patients dependent on cocaine, we undertook a study of the relationship between severity of cocaine dependence and 3-month treatment outcome.

One-way analysis of variance (ANOVA) was used to assess the relationship between outcome and interval variables. Chi-square analysis was used in the assessment of the relationship between outcome and nominal variables.

METHOD

Data were collected from 52 patients hospitalized for treatment of cocaine dependence, which was diagnosed

by using the Structured Clinical Interview for DSM-III-R (SCID) (6); all patients gave informed consent. We eliminated from our analysis seven patients who had another axis I diagnosis that antedated their substance use disorder because comorbid psychopathology may influence treatment outcome in drug-dependent patients (7, 8). Six subjects were lost to follow-up. Our final study group thus consisted of 39 patients.

Severity of cocaine dependence was measured as a function of the number of criteria met for that diagnosis in the psychoactive substance use disorders section of the SCID, which was generally administered during the second week of hospitalization. A patient had to meet at least three of nine possible criteria to be given a diagnosis of dependence on a particular drug. Rather than using the subjective distinctions among mild, moderate, and severe dependence listed in *DSM-III-R*, we measured severity according to the number of diagnostic criteria met. For example, we considered a patient who met six criteria to have more severe dependence than a patient who met five criteria.

Follow-up assessments included monthly administration of the Addiction Severity Index (9), urine toxicological screens, and weekly substance use questionnaires. A repeat SCID was obtained at 3 months.

We divided treatment outcome into three categories: 1) total abstinence, 2) a slip, which we defined as having used cocaine on 1-3 days in the previous 3 months (i.e., 1 day a month or less) but not using cocaine at the time of the 3-month assessment, and 3) relapse to cocaine dependence.

RESULTS

The study group was predominantly white (N=34, 87%) and employed (N=27, 69%), with a slight preponderance of men (N=21, 54%). The patients had used cocaine for a mean of 8.8 years and had previously engaged in inpatient treatment a mean of 1.2 times. Twenty-one (54%) of the patients were predominantly intranasal users, 15 (38%) used cocaine primarily by

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TABLE 1. Relationship of Severity of Cocaine Dependence to 3-Month Outcome in 39 Hospitalized Patients^a

Outcome	Number of Cocaine Dependence Criteria Met ^b	
	Mean	SD
Abstinence (N=24)	7.1	1.3
Slip (≤ 3 uses of cocaine) (N=6)	7.3	1.0
Relapse to cocaine dependence ^c (N=9)	8.0	1.2

^aF=1.67, df=2, 38, n.s.^bBased on DSM-III-R criteria for cocaine dependence in the psychoactive substance use disorders section of the SCID.^cNo patients relapsed to dependence on another drug (including alcohol) in the absence of cocaine use.

smoking, and three (8%) were intravenous users. The patients were currently using a mean of 16.7 g of cocaine per week and had spent, on average, \$7,250 on cocaine during the previous 6 months. There was no significant relationship between any of these cocaine use variables and 3-month outcome.

SCID data revealed that most of the patients (N=32, 82%) met criteria for at least one other current substance use disorder, particularly alcohol abuse or dependence (N=23, 59%). Among the patients with both cocaine dependence and alcohol abuse or dependence, 11 (48%) met criteria for a third substance use disorder. Subjects lost to follow-up were determined to be no different from available subjects with regard to sociodemographic characteristics, substance use histories, or number of SCID criteria met for cocaine dependence.

The mean number of SCID criteria met for cocaine dependence was 7.4 (SD=1.2) (range=4–9). As shown in table 1, ANOVA revealed no significant relationship between the number of criteria met and 3-month outcome. Grouping patients who had used cocaine three or fewer times during the 3-month period with abstainers, relapsers, or by themselves did not affect this result.

We reanalyzed our data by categorizing patients as having low, moderate, and high levels of severity. We measured severity in two ways according to the number of criteria they met: 1) mild=4 or 5 criteria, moderate=6 or 7 criteria, and severe=8 or 9 criteria, and 2) below the median=4–6 criteria, median=7 criteria (also the mode), and above the median=8 or 9 criteria. Neither measure of severity was significantly related to outcome.

DISCUSSION

Our data suggest that either 1) counting the number of DSM-III-R criteria met for cocaine dependence is an inadequate measure of severity or 2) severity of the cocaine dependence syndrome per se is not a good predic-

tor of future cocaine use. Our findings, combined with those of Babor et al. (5), who found that severity of alcohol dependence but not severity of opioid dependence was a good predictor of relapse, suggest that measures of severity of dependence may be somewhat substance specific.

Babor et al. (5) found that the drug severity score on the Addiction Severity Index was a significant predictor of the severity of the follow-up dependence syndrome in opioid addicts, although the correlation was not high. We did not report Addiction Severity Index scores in this study because Addiction Severity Index ratings of drug severity do not clearly distinguish among drugs. Because of the high rate of polysubstance abuse in our subjects, we focused specifically on the severity of cocaine dependence in this report.

One limitation of our study was the narrow range of severity scores in our subjects; since this was a hospitalized group of patients, most of the subjects had quite severe cocaine dependence. Moreover, findings in this study group of primarily white, employed patients may or may not be generalizable to cocaine-dependent patients in other settings. Future investigations that examine larger and more heterogeneous patient populations (e.g., minorities, unemployed patients, outpatients) are needed to help us make the measurement of severity of cocaine dependence a clinically useful tool in predicting clinical outcome and developing successful treatment strategies.

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Book Forum

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CHILDREN AND ADOLESCENTS

The Course of Life, vol. 4: Adolescence, edited by Stanley I. Greenspan, M.D., and George H. Pollock, M.D., Ph.D. Madison, Conn., International Universities Press, 1991, 519 pp., \$60.00.

Adolescence, one of the most crucial phases of development in the human cycle, is approached in this volume in a most interesting way, like a corridor with many doors. We have the contribution of Peter Blos reviewing the role of the father in pre-oedipal or early male adolescent development. Blos deals with the heretofore ignored early relationship between father and son, which provides the boy a particular sense of emotional and physical security and safety.

Further subdivisions and elaborations on the substages of adolescence are given new insights and knowledge. Thus we have the work of Judith Kestenberg on the transition from childhood to adolescence, followed by several papers that elaborate on the passage from late adolescence to early adulthood. This book contains important and controversial issues connected with the homosexual adolescent and his development. It would have enriched this area of the volume if other psychoanalytic researchers, such as Richard Freidman and Susan Coates, would have contributed.

Although there is overlap in the chronological substages, this text illuminates the issues that adolescence brings out in terms of potential for disturbance and psychopathology, such as the Hilde Bruch's concept of "escape from change" in her sleeping beauty metaphor. The book also focuses on the insights into developmental psychology provided by the study of adolescent delinquents, as illustrated by Shore and Massimo. There are some innovative detours into a discussion of the relationship between family dynamics and learning disorders and a discussion of career achievement, issues that have not been tackled in other comprehensive textbooks of adolescent development. Daniel Offer contributes normative perspectives and an important caution to avoid the previous decades' mistake of considering adolescence a period of heightened psychopathology.

One issue that I did not see developed as it deserves is the complex interplay between suicidality and adolescent stages. It is not included in the subject index. I am sure that many of the authors have much to say about this important topic from a psychoanalytically inspired developmental perspective.

I consider this volume a welcome complement to traditional descriptive psychiatry. In my opinion, it is impossible to really understand psychopathological syndromes in adolescence without having grasped in depth the subjective experience of adolescents in their psychological structures—the working schemata formulated by adolescents to deal with themselves and others. In summary, this book is an enriching source to be recommended to anybody interested in human develop-

ment in general and high school and college-age populations in particular.

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Fundamentals of Child and Adolescent Psychopathology, by Syed Arshad Husain, M.D., F.R.C.P.(C), F.R.C.Psych., and Dennis P. Cantwell, M.D. Washington, D.C., American Psychiatric Press, 1991, 316 pp., \$45.00.

This book by Drs. Husain and Cantwell is a fundamental text of child and adolescent psychopathology. It is written for students of medicine and allied disciplines, not for specialists in child and adolescent psychiatry. The guiding framework for the description of the disorders in this book is APA's *DSM-III-R* classification system. In this system, disorders are first described phenomenologically and then are defined by inclusion and exclusion criteria. The system also emphasizes subtyping and differential diagnoses. The conceptual implication of such a system is that these clinically defined disorders will differ in demographic factors such as age, sex, and social class; in prevalence rates; in morbid risk rates and life expectancy; and in outcome and response to different forms of therapeutic intervention.

The text is divided into three sections. The first, Introduction, comprises five chapters that discuss the history of child psychiatry; normative development focused on attachment and bonding, Piaget's cognitive development, Erikson's psychosocial development, gender identity, moral development, and temperaments; principles of assessment and tools for the assessment; purposes of and a theoretical approach to classification and elements of the *DSM-III* system of diagnostic classification; and types of therapeutic interventions and principles of psychopharmacotherapy in child psychiatry.

The second section, Disorders, consists of 11 chapters focused on childhood and adolescent psychiatric disorders, including disruptive behavior disorders, anxiety disorders, eating disorders, tic disorders, elimination disorders, speech disorders not elsewhere classified, mood disorders, suicide, parasomnias, developmental disorders, and other disorders such as elective mutism, identity disorder, and reactive attachment disorder. For each disorder there is a brief description or discussion of the clinical picture, natural history, etiology, epidemiology, differential diagnosis, and treatment.

The third section, Psychiatric Symptoms, Chronic Conditions, and Special Problems, contains three chapters dealing with common psychiatric symptoms that are not part of any psychopathological disorder per se (e.g., thumb and finger sucking, masturbation), psychiatric symptoms associated with chronic medical conditions (e.g., asthma, cancer, and deafness), and special problems such as physical and sexual abuse and death and dying. The meanings of the symptoms in these conditions are briefly discussed, and useful managements are described.

Although neurobiological studies have not been validated, this book refers to some recent developments in genetics, neurochemistry, neuroimaging, and neuropharmacology in child and adolescent disorders. These developments and the therapeutic interventions of each disorder are not discussed in great detail, but an overview is given for each disorder, followed by references for further reading. It is somewhat disappointing that more recent data were not incorporated; there are no clinical references past 1989, and many of the references cited were published in the 1950s, 1960s, and 1970s. This certainly does not give one an impression that child and adolescent psychiatry is a fast-growing medical and behavioral science.

The book is well written, and the authors are to be congratulated on the massive amount of careful work that has gone into its production. It has a great deal to offer the beginner as a good first step toward an understanding of the fundamentals of child and adolescent psychopathology. If the reader wants an easy-to-read book that reviews and integrates the research literature, this is an excellent book to have until the *DSM-IV* classification is adopted.

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PSYCHOANALYTIC VIEWS

The Fundamentals of Psychoanalytic Technique, by R. Horacio Etchegoyen; translated by Patricia Pitchon. New York, Brunner/Mazel, 1991, 863 pp., \$100.00.

This unique and very long book, written by a brilliant man and an astute clinician, poses a reading task similar in my mind to Tolstoy's *War and Peace*. Of course Etchegoyen would say that my association to *War and Peace* reflects my ambivalence about his book, and he would be correct. The book is interesting and erudite and packed with many clinical insights and theoretical speculations, but as a reviewer I must also point out some of its serious flaws.

The book comprises Etchegoyen's informal talks to his students interspersed with his reading notes, so it presents a mixture of fascinating clinical anecdotes, personal opinions, and very condensed reviews of some extremely difficult authors. One of the remarkable aspects of the book is that the authors reviewed are writers in several languages, and some of them will not be familiar to U.S. psychiatrists and psychoanalysts.

Etchegoyen is a prominent Argentine psychoanalyst and an important personage in international psychoanalysis. His writing makes it obvious that he has a complete grasp of the Kleinian theory he espouses and great clinical experience along with impressive intuitive skill. This book desperately needs editing because it is quite repetitious and many of the sentences are cumbersome. I do not know if this is a function of the translation or not, but the reader will have to be prepared to tangle with such syntactical catastrophes or obscure ambiguities as,

Since Winnicott never leaves out of consideration the genetic equipment of the newborn child, then inevitably the thought is that the child influences his environment (mother), with which we are already supporting the Freudian idea of complementary series that Klein utilizes, questioning at root the doctrine of environmental failure, which the child has nothing to do with. (p. 562)

As a third possibility, Money-Kyrle studies the orientation towards a confused base and takes Meltzer's (1966) paradigm, when the child confuses the mother's breast with the bottom that goes away and then with his own bottom, which he enters in a masturbatory act. (p. 777)

Eight hundred pages of this leave the reader exhausted. The historical and current literature reviews that appear in each section are obviously dictated directly from reading notes and not always well integrated with the text (for example, the reviews of Yorke on pages 400–401 and Caddini on pages 722–723). I do not believe the discussions of such important thinkers as Lacan and Bion can be understood by anyone who is not already familiar with these writers, and this is true of the reviews of a number of other thinkers that are interspersed throughout the book. The informal chatty style, when it appears, is very enjoyable, but it is not always clear whether Etchegoyen believes what the author he is reviewing believes.

The book is in essence a polemic for Kleinian psychoanalysis, and some parts, especially the case vignettes, are very well written and reveal Etchegoyen to be a clever, decent man and an outstanding psychoanalyst, but the appreciative audience for the book would have to be primarily experienced psychoanalysts. Even psychoanalytic candidates would have trouble with it because they do not have the necessary background to engage with Etchegoyen in his theoretical discussions.

The book really is two books in one. The first consists of Etchegoyen's review of the literature and theoretical discussions, and the second propounds his approach to the technique and practice of psychoanalysis. Both are extremely valuable, but the former requires much more reading background and knowledge than the latter.

Etchegoyen indulges himself in some extraordinary statements that are put forward without documentation, for example, "Ulcerative colitis . . . even in its most serious forms, is an illness that almost always responds satisfactorily to psychoanalysis" (p. 22). He also likes to throw in references to philosophers, which are both dubious in content and will be completely unintelligible to readers who are not familiar with the philosopher. For example, he tells us, "In this sense, if it is successful, analysis resolves dialectically Heidegger's three stases of time" (p. 91). Not only will this be meaningless to anyone who has not studied Heidegger's *Being and Time*, but I believe those who have studied *Being and Time* will disagree, because Heidegger's *ek-stases* of time are part of his ontological investigation, and he would not be willing to apply this to ontic studies such as psychoanalysis. It is not clear why the chapter by Klimovsky "Epistemological Aspects of Psychoanalytic Interpretation," was included in the book, since it ignores a vast literature on this topic and certainly does not contribute anything to understanding the fundamentals of psychoanalytic technique.

Etchegoyen's Kleinian orientation requires the reader to accept such speculations as those about the effect on an adult woman of her mother's nipple being cracked during her infancy or about the effect on a male patient of his mother's milk suddenly drying up when he was 2 months old. It might be felicitous to read Etchegoyen at his best by starting with the clinical cases presented on pages 287 and 363, which demonstrate his version of Kleinian psychoanalysis in action. If the reader cannot accept such speculations about the infant's experiences and their effect on the adult, then the reader will be unable to tolerate this book. In Cervantes' great novel, there are two paradigmatic characters in a dialectic, Don Quixote and Sancho Panza. The Kleinians with their wonderful imagi-

nation may be thought of as the Don Quixotes of psychoanalysis, and the American pragmatic ego psychologists may be thought of as the Sancho Panzas. The polemic between the two is a theme running throughout Etchegoyen's book, and he attempts to be fair to the Sancho Panzas, although clearly he is a Don Quixote, when he is not writing like Thomas Aquinas, as he does in chapter 8, his scholastic commentary on Freud's "The Dynamics of Transference."

Etchegoyen is a superb clinician and very conservative: "No intervention of the analyst is valid if it violates the rule of abstinence" (p. 13). He leans heavily on Bion's idea of *reverie*, a capacity for resonance with what the patient projects. Etchegoyen is a humane physician with good common sense and decency in his treatment of patients. He insists that there is no effect of tape recording and note taking during sessions, which I find puzzling, for just as he says that "transference exists in everything" (p. 83), I am sure he is well aware that countertransference exists in everything also.

Because Kleinians emphasize the intrapsychic fantasy life of the baby much more than the actual environmental factors, Etchegoyen cannot accept Kohut's basic contention that parental failure of empathy is the crucial pathogenic factor in narcissistic disorders. This is not to revive the incorrect argument against the Kleinians that they do not take into account environmental factors at all. In fact, the case histories on pages 287 and 363 hinge on postulated unfortunate environmental happenings. Etchegoyen also rejects the common complaint that Kleinians interpret too deep and too fast, which implies that Kleinians have no common sense. I think he is correct about this. In a book with many case vignettes I found only one (p. 547) where I thought Etchegoyen really missed what was going on.

I did not find Etchegoyen's explication of Racker's views to be intelligible, and I had the same problem with the long and tedious discussion of Money-Kyrle's theories, which takes up much of chapter 59. On the other hand, I found the discussions of projective counteridentification, negative therapeutic reaction, acting out, and Bion's "reversible perspective" to be excellent and clinically very valuable. Etchegoyen's emphasis on separation anxiety, which comes up repeatedly in the latter part of the book, is very important for clinicians. I found the attempt to differentiate between projective identification and "adhesive identification" as a form of "very narcissistic" (p. 574) identification provocative but questionable. One emerges from Etchegoyen's book with an increased appreciation of the work of Bion, since Etchegoyen seems to have thoroughly integrated Bion's thinking into his technique. This is especially true in the discussion of "the container/contained theory," but readers will have to accept Bion's Kleinian insistence that "we are born with a *preconception* of the breast" (p. 587).

In spite of his reliance on Popper, Etchegoyen makes the valuable clinical point that "the analytic process continually tests the theories the analysand has about himself and leads him to confront these with the content of reality" (p. 683). This is an excellent way to look at the concept of insight, and it leads into a discussion of the obstacles to insight as Etchegoyen lists and discusses them—acting out, negative therapeutic reaction, and reversible perspective.

The reader will have to decide whether this book accomplishes what Etchegoyen calls its "most persistent purpose," which is "to draw a clear distinction between psychoanalysis and any hidden or overt way of psychotherapy, through a model that respects the internal life of the analysand and abstains rigorously from suggestion and direct action, however beneficial it may appear to us" (p. 803). The book is a unique

and fascinating personal statement by an extraordinary man, but it is not to be considered a basic book on the technique and practice of psychoanalysis comparable, for example, to the well-known work of Greenson (1) or the meticulous text by Thomä and Kächele (2). It is best read as a brilliant example of an experienced Kleinian analyst at work, interspersed with a review of the international literature at an advanced level. Anyone who is willing to yield at least temporarily to the quixotic Kleinian imagination and is willing to struggle with the difficulties of this text is certain to emerge with an improvement in their clinical work and with some fresh ideas on their theoretical orientation. I hope this book will soon appear in a second and rigorously edited edition, which will make it accessible to the much wider audience that it well deserves.

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Pain and Passion: A Psychoanalyst Explores the World of S & M (Sadomasochism), by Robert J. Stoller, M.D. New York, Plenum, 1991, 306 pp., \$24.95.

This book is a masterpiece. It is an informative contribution to the science of human behavior. Dr. Stoller, who died last year, was Professor of Psychiatry at the University of California, Los Angeles, a psychoanalyst, and an authority on gender identity, erotics, and perversions. With courage and curiosity, in this book he presents personal observations of strange sexual human practices, some places where they occur, and their operations.

In the preface, he relates how he entered the natural habitat of practitioners of bondage and discipline to learn in depth about what is "normally" considered repugnant and bizarre human behavior. He emphasizes the need while reading this book to be alert to what is true and valid.

The book contains five parts. The first, Introduction, consists of three chapters: "Consensual S.M. Perversions," "The Term Perversion," and "Methodology." In discussing ethnography Dr. Stoller says, "I want to do something risky—in pulling the decent reader to primitive raw data" about Sadomasochism. He insists that natural observations are essential before deciding on psychoanalytic theory. The place for observation is the bondage and discipline establishment to obtain information from owners, employees, habitués, sadomasochism therapists, and pornographers.

The term "perversion," according to Dr. Stoller, involves genital excitement by means of pain. He presents a long classified list of perversions and cautions that true dangers must be prevented in the theatrical increase of excitement. This entails mutual trust of partners who know and observe the rules of dehumanization and avoid nonconsensual acts like rape. Dr. Stoller points out that the participants appear "sick" in a single aspect of sexual life but are otherwise "normal."

In the chapter on methodology Dr. Stoller tells us he worked without a plan. His purpose was to get acquainted with his surroundings, ask people what they think, and stimulate them with interesting questions. The accuracy of their responses cannot be checked. He audiotaped all interviews, wrote up the

material, let the people involved read and correct his material, reviewed the literature, and cross-checked. He questions whether this is scientific.

Part two, *Ethnographic Joys*, contains four chapters: "Entree," "Dominatrix and Slave," "An Island for Dr. Moreau," and "Ladies Club." In the first chapter, Dr. Stoller says that the police provided entree to legal bondage and discipline clubs. Dr. Stoller learned that advertisements for bondage and discipline appear in the press. Some establishments offer tours for the customer, and tours were arranged for him. He describes one house he visited as looking like a home with special rooms made up theatrically with instruments of torture. Dr. Moreau, the owner, says that his customers are just folks playing out erotic fantasies without orgasm and that he is committed to erotic pleasure and has even tried to obtain research grants for such studies. In this house, Dr. Stoller sees a woman in diaphanous clothes prepared to be beaten by a man or to beat him. He tells us that the death instinct or aggression turned inward is insufficient to explain such practices. Max, the owner of another bondage and discipline club, considers it a business. Dr. Stoller emphasizes that he is informed only of surface behavior, not what people are thinking in depth. He describes Tammy, a sexy female professional who shows him instruments of bondage, torture, and degradation. While speaking to him, she pinches his nipple to demonstrate her talent, but he protests and she stops. Tammy tells him she is dominant toward males but is capable of switching to being submissive, that Stanley is her slave, that she slaps his face and he loves it. Candy, a seductively dressed childlike female, shows off stripes of having been beaten.

In the chapter on dominatrix and slave Dr. Stoller describes listening to a videotape and his concern about what the truth might be. Further information about Tammy's dominance reveals her as a femme fatale in spike heels looking for submissive males for bondage and discipline. Slaves do her chores and sexual biddings, receive her punishment, and worship her. She is involved with fetishes, both soft (silk, satin, and nylon) and hard (leather, spandex, and rubber). Her object is to degrade men, tease them, overpower them, and turn them on, all without orgasm. If the consensual agreement is violated by the customer, she threatens with a controlling admonition, "If you do that again, you'll lose your cock," and they stop. Excitement comes from the act of submission and is not considered sexual.

In another chapter in this section, Dr. Moreau is described as a philosopher and theoretician referred to as "sir." He and several of his employees provide information. For instance, Bart loves sadomasochism because of its honesty and feels that it is less hostile than sexuality expressed among "normals." Honey declares that the feminine erotic preference is to be submissive to a dominant male. She insists that all women look for this dominant male. Employees of the club are selected carefully. They must have above-average intelligence, and hookers are excluded. The customers are not freaks. Female clients are articulate and assertive and include doctors, lawyers, designers, and executives. They seek submissive bondage, especially nipple clamps, for excitement. There is an alarm system to which the staff respond immediately to protect female clients against aggressive men who may violate consensuality. The staff can be rough in their assistance. Male clients include judges, lawyers, doctors, and police officers. Some may encourage their wives and girlfriends in bondage and discipline practices, and the hope is that they will come ultimately to rent a room.

In "Ladies Club," Dr. Stoller tells us that Dr. Moreau does not let him talk with some women who want to talk to him.

Dr. Moreau is also unforthcoming regarding details and explanations of his philosophy. Max, too, is guarded and uneasy and presents superficial undynamic information. A third discipline and bondage club is owned by two women who talk about the glories of bondage and discipline and defensively try to elevate their self-esteem. In addition to the usual instruments of torture, this club contains cages for further dehumanization. The setting is noisy, cluttered, public, and uncomfortable, with competing informants resulting in incoherent dictation. They tell Dr. Stoller that Dr. Moreau is crazy, that he can no longer tell fantasy from reality. The atmosphere is whorish and fetishistic, operated by smart women who say they are helping people. Dr. Stoller wonders how to tell truth from fiction, whose report to believe, and what has been forgotten, omitted, or discounted as unimportant in providing narrative descriptions.

Part three, *Recitativos*, consists of three chapters, "How One Plays," "Dominatrix Redone," and "Dominatrix." In the first of these chapters Dr. Stoller declares that the main purpose of the book is to determine criteria of validity. His informant, Ron, impresses him as articulate, insightful, and honest. Ron is a writer, is in therapy for manic-depressive disorder, and likes pornographic films. He declares that life in the clubs is unstable, that entrepreneurs take advantage of vulnerable employees. Actually, all of the clubs are houses of prostitution, but the women do not consider themselves whores. They are poor, have little education, are damaged psychologically, and have low IQs. Clients lie and are perverts and kinks, but most are scared and respectful. The police have to be called in to control dangerous clients.

In "Dominatrix" Stoller discusses Tammy again. She is open, intense, erotic, manic-depressive, suicidal, and has a need to be hurt. She lives with Ron, who fulfills this need, and she is affectionate toward him in response. When she is bad to him, she begs him not to hate or abandon her. She trades sex for cocaine, and she likes being chained down so that she can overcome her cocaine binge. Ron turns her from dominant to submissive and he whips her while a client watches. She would like to be normal. Her family history is one of emotional disorder. During an interview of a male client, she determines his wishes and negotiates the cost. She sets up a slave set and does everything to hurt and humiliate him. When he screams theatrically, "I'm going to die," she induces more pain, pinching his nipples, and has an orgasm on his face. Shortly after, Tammy has a suicidal cocaine episode.

Part four, *S & M Porn*, consists of the chapters "Merlin of the Movies" and "Merlin Magus Magister." Merlin lives dangerously yet cautiously. He has been a high school teacher and does not look cruel. He writes, produces, directs, and performs with Ron and three women in pornographic films. The men feel that they are rebels against a straight society and enjoy forcing decent folk to discover their own pornographic propensities. It is all simulation and fantasy, a game of erotic day dreams and feelings that men cannot share with their mates. Can films seduce viewers? Intelligent people are attracted to sadomasochism, and they seek more variety in sex. In Ron's opinion, people in sadomasochism have no domestic violence to overcome. They have fantasies based on adult erotics, and pornographic production should be legal. Actress Vanessa declares that sex is her business and her task is to provide excitement and gratification for men.

In part five, *Conclusion: Ends and Starts*, Dr. Stoller presents thoughtful comments about the complexities of psychiatric work and the necessity to question whether what is reported by informants is to be trusted. Our object is to learn more than we know about perversions and to learn to judge

what is written. He suggests that perversion is an eroticized triumph over childhood traumata—a triumph over evil and self-deception.

Dr. Stoller made a fascinating house call to extend the work of Krafft-Ebing, Ellis, and Freud, and although he doubted the science of his work, I think he applied its major first step—observation. He exposed himself to a strange aspect of human behavior without fear of “catching it.” He did not actually see the bizarre in action, and maybe that is for the best. I am deeply impressed with his work, not only for medical reasons but for its forensic value. It should be studied by all mental health professionals and those legal minds interested in perversion. The final chapter certainly should be studied by students of science. The book contains a bibliography and an index. Read it.

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TEXTBOOKS

The American Psychiatric Press Textbook of Neuropsychiatry, 2nd ed., edited by Stuart C. Yudofsky, M.D., and Robert E. Hales, M.D. Washington, D.C., American Psychiatric Press, 1992, 805 pp., \$95.00.

Neuropsychiatry is gradually coming of age. Its major aim has always been to link abnormalities in cognition, mood, and behavior with specific brain dysfunction. In the late 1960s and early 1970s, most study of neuropathologically caused disorders of behavior or intellect focused on aphasia, apraxias, amnesias, dementias, and complex partial seizure disorders (“temporal” and “frontal” lobe syndromes were often discussed in this latter context). These areas often fell under the rubric of “behavioral neurology,” which was largely rooted in relationships between structure and function based on neuroanatomical lesions and seemed more neurology than psychiatry. At this time, the nascent discipline of biological psychiatry, with its roots in psychopharmacology, the chemical “soup” of the brain, seemed a distant cousin. Biological psychiatry sought to explain more complex behavioral abnormalities and make pathophysiological inferences by reasoning backwards from the known biochemical actions of effective psychopharmacological agents. Students of one discipline seldom knew a comparable amount about the other.

As biological psychiatry became increasingly informed by an exploding neuroscience database in the 1980s, neuropsychiatry, still heavily based on clinical-anatomical correlations (and often small-scale anecdotal ones at that), seemed to be lagging behind. I purchased the first edition of this book shortly after its 1987 publication and found myself disappointed, though not surprised. It was heavily focused in clinical-neuroanatomical correlations and included little in the way of recent developments in neuroscience. As such, it resembled a smaller scale, far less comprehensive version of Lishman’s textbook *Organic Psychiatry* (1).

When I saw this second edition of *The American Psychiatric Press Textbook of Neuropsychiatry*, I was shocked, surprised, and delighted. Almost twice the size of the first edition with 15 totally new chapters and 10 chapters entirely rewritten by new authors (only eight original chapters remain and even these have been revised and updated), this is a totally new book. To begin with, the organization has changed substantially. From three sections, some with conceptually mixed

messages, it has gone to five crisp, orthogonal sections: 1) Basic Principles of Neuroscience, 2) Neuropsychiatric Assessment, which includes the bedside examination, neuropsychological testing, electrodiagnosis, and brain imaging (the epidemiology and genetics chapter, though superb, is out of place here and seems to belong back in the basic section), 3) Neuropsychiatric Symptomatology (this section should be labeled “Syndromes”), addressing disturbances in attention, sensation (pain), language, memory, mood, impulse and mixtures of these (delirium) in both pathophysiological and biochemical terms, 4) Neuropsychiatric Disorders, organized around etiologies such as infection, trauma, metabolic, stroke, tumor, and degenerative dementias, and 5) Neuropsychiatric Treatments, the only section still reasonably intact from the first edition (and one of its best).

An editorial board of superstars (Andreasen, Barondes, Bloom, Coyle, Cummings, Robinson, Snyder, and Tucker) obviously allowed more stringent peer review, and it shows in the overall scope, depth, and critical detail of each chapter. The citations at the end of each chapter are of unusually high quality and currency. Although each of the chapters is unique in its own way, there is a degree of redundancy throughout that allows for different perspectives on a specific topic. However, each chapter stands on its own as a comprehensive review. Throughout the book, pathophysiology from both gross anatomical and more microneuronal/transmitter perspectives is emphasized, and the solid clinical detail of the first edition is retained. This interweaving of the basic and clinical builds in a major strength. Most importantly, intelligent theoretical discussions of potential pathophysiological mechanisms in cases where brain pathology cannot be technologically demonstrated allows clinicians to “find their way in the dark” by refining their intuition and judgment about specific cases and syndromes where there may be a dearth of information.

In this edition, the 88-page, three-chapter section on basic principles of neuroscience replaces a single 35-page chapter in the first edition that reviewed concepts of neuronal transmission focusing on the classical transmitters circa 1980. Here, in chapter 1, stupendous illustrations supplement readable but not simplistic discussions of neuronal signaling, postsynaptic receptor mechanisms, sensitization, long-term potentiation, and neuronal growth and plasticity. Chapter 2 discusses the electrophysiology of sleep, arousal, and wakefulness, focusing on excitatory amino acids, second messengers such as calcium, and the role of early gene expression (c-fos and jun). Chapter 3 is a solid basic review of functional neuroanatomy based mostly on human lesion studies.

The section on assessment has done away with speculative attempts of the first edition to include “biomarkers” such as thyrotropin-releasing hormone testing and platelet receptors as part of the assessment battery and instead improved on its discussion of imaging. One can read in a brief, succinct section about the meaning and clinical significance of T₁- or T₂-weighted magnetic resonance images and find a careful, terse review of positron emission tomography findings related to the major psychiatric disorders. Magnetoencephalography is briefly discussed, and the uses and limits of EEG “brain mapping” are cogently reviewed. The bedside testing chapter is far broader in scope than before, although inclusion of assessment scales besides the Mini-Mental State Examination might have been helpful for the clinician.

In the third section, discrete syndromes are discussed from anatomical, physiological, and biochemical perspectives. Although the chapters are uniformly solid, the general organization of each is quite different, making the section itself appear disjointed when several chapters are reviewed in succession.

The extreme opposite would be *Harrison's Principles of Internal Medicine* (2), where symptoms are all reviewed based on the same general outline. This section, instead, strives to leave the individual stamp of each author on its chapters, which has its drawbacks. A particularly strong chapter is the one on delirium by Wise and Brandt. It has been updated considerably and is now more strongly data based, with studies rather than cases included wherever possible. As such, it is the best general review of delirium I have seen.

In the fourth section, specific neuropsychiatric disorders are reviewed. Many of these chapters were retained from the first edition. Among the stronger ones in that edition, they have been further updated and revised. In particular, the chapter on head trauma by Dr. Silver and the two editors, Dr. Hales and Dr. Yudofsky, considerably expands the discussion of clinical features and methods of assessment. Although it makes timely mention of the difficulty distinguishing past concussive versus posttraumatic stress disorder aspects of head injury, more discussion of this would have been useful. The chapter on cerebrovascular disease has also been further refined, and more clinical information and more background studies have been added. A section in the first edition on neuropsychiatric aspects of vitamins is now gone, which is too bad, although its relevance to the practicing clinician may have been limited. A new chapter on AIDS is timely and required reading for any general psychiatrist. In addition to basic virological mechanisms and a review of opportunistic CNS infections, it has an excellent discussion of the controversial area of neurocognitive deficits in early HIV infection, in which the authors, rather than drawing firm conclusions, provide a scholarly framework for analyzing the disparate results of individual studies in this area. The chapter on alcohol-induced disorders has, in addition to predictable discussions of both withdrawal and Korsakoff's syndrome, a more novel review of neuropsychological changes in alcohol abusers not suffering from Korsakoff's, which is quite clinically relevant. Despite its admirable scope, the chapter on epilepsy, in an attempt to go beyond the fairly straightforward, unambitious one in the first edition, strays too far from the data in places and relies too heavily on opinion, anecdote, and the introduction of acronyms. For the first time, schizophrenia takes its place among these other, more traditionally neurological disorders with its own chapter. Although the data reviewed are comprehensive and up-to-date, the conclusions are necessarily preliminary and vague ("the exact neuropsychiatry of schizophrenia remains a mystery"), suggesting that these more complex behavioral disorders, while theoretically the province of neuropsychiatry, will continue to stand somewhat apart from it.

The final section on treatment remains as before, solid, but also new and improved. A chapter on the psychology of neuropsychiatric disorders is outstanding, and a new one on family caregivers of afflicted patients is timely with the increasing research in this area. A single chapter on psychopharmacology is an impossible task that is reasonably well accomplished, especially since this topic appears in many other chapters with respect to given syndromes and disorders. Finally, a newly authored chapter on ethics and legal issues in psychiatry written by Robert Simon, editor of the *American Psychiatric Press Review of Clinical Psychiatry and the Law* series (3), is outstanding.

I have traditionally counseled residents and junior faculty members to avoid purchasing most textbooks. Although they often provide an easily accessible source of information, not infrequently the treatment of a given topic can be out-of-date, too superficial, overly weighted in the basic science or clinical

direction, idiosyncratically skewed by the author's own research or clinical interests, and lacking discussion of a key concept or area. In my mind, this book, though not perfect, is an exception. The editors are to be commended for bringing the field of neuropsychiatry up-to-date with the rest of neuroscience, while still making it wholly accessible to the practicing clinician. This was no easy task.

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Inpatient Psychiatry: Diagnosis and Treatment, 3rd ed., edited by Lloyd I. Sederer, M.D. Baltimore, Williams & Wilkins, 1991, 431 pp., \$58.00.

This is the third edition of a valuable textbook first published in 1983. The fact that it is a third edition in less than 10 years attests both to its value to the field and the rapidity of change in psychiatry that necessitates frequent updating of standard texts. Like the previous editions, this version is divided into two major sections, one dealing with the diagnosis and treatment of specific diagnostic entities and the other with specific aspects of inpatient treatment.

Compared with the first edition, most of this volume is new material by new authors. Only six of the contributors to the first edition are represented in this revision. In section one, most of the same topics are included and an excellent chapter on HIV Infection by Marshall Forstein and Jay Baer has been added. In section two, new chapters by Bursztajn, Gutheil, and Cummins ("Legal Issues in Inpatient Psychiatry"), Schwartzberg and Kahane ("Occupational Therapy"), and Sederer ("Quality, Cost, and Contracts: Administrative Aspects of Care") are included.

Treatments such as psychotherapy, milieu, group, psychopharmacology, family work, and others are covered in each of the chapters in section one. Although this allows for a tailored discussion of approaches to each disorder, it also leads to redundancy. Some chapters are repetitious; for example, there is considerable overlap between the chapter on organic mental disorders in section one and the chapter on the clinical laboratory in section two. The inclusion of discussions of controversies in treatment for each disorder provides a forum for a broader look at the practice of hospital psychiatry.

This volume focuses on acute inpatient care and is probably more pertinent for psychiatrists and others working in private hospitals or on acute psychiatric units in general hospitals. It does not offer much for the treatment of the chronically ill public mental health patient. For example, discharge planning and aftercare planning are not discussed. Nor are the topics of water intoxication, posttraumatic stress disorder, or multidisciplinary treatment planning covered. The treatment plan has a single reference in the appendix to the chapter on the medical record. This refers to the team treatment plan as "the operational core of the chart and the veritable compass of the course of hospitalization" (p. 417). In view of the absence of

discussion of treatment planning elsewhere in this volume this is a hollow assertion. Accreditation issues are not mentioned, although quality assurance and utilization review are. The absence of a section on geriatric psychiatry is surprising and distressing in view of the fact that the elderly are one of the faster growing segments of inpatient populations. These are minor criticisms; to deal adequately with issues of importance to the public sector inpatient setting would require a book twice as long as the present one. Regardless, this is a useful book that deserves to be on the shelf of every psychiatrist who practices in a hospital setting.

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ALCOHOLISM

Recent Developments in Alcoholism, vol. 9: Children of Alcoholics, edited by Marc Galanter. New York, Plenum, 1991, 350 pp., \$72.50.

The goal of this and previous volumes in this prestigious series is to examine subjects in alcoholism that are timely and challenging. This volume begins with a section entitled Genetic Predisposition to Alcoholism, which examines in detail a number of psychological and biological factors in individuals at highest risk. The second section reviews the fetal alcohol syndrome. Facts and medical syndromes are described in sufficient detail for the clinician and researcher. Estimates of the treatment cost to our society per year for fetal alcohol syndrome may be as high as \$53 billion. The third section of the book considers alcoholism and vulnerability to disease. Alcohol is known to suppress the immune system, making alcoholics vulnerable to many transmissible diseases. The final section reviews social and environmental issues with a special emphasis on the epidemiology and psychological characteristics of children of alcoholics and adult children of alcoholics.

The editor, Marc Galanter, has done a wonderful job of inserting considerable order into this volume. The four major sections are successfully introduced by a state-of-the-art overview. Henri Begleiter (Genetic Predisposition to Alcoholism), Donald Gallant (Fetal Alcohol Syndrome), David Van Thiel (Vulnerability to Disease in Relatives of Alcoholics), and Edward Gottheil and Jeannette Johnson (Social and Environmental Issues) conscientiously describe what is included in their section and why. The individual chapters within these sections are remarkably well-written and superbly edited. In general, these chapters are uniformly organized with an introduction, topical reviews, conclusions, and references. This volume is well-suited for reading as well as a reference text because the table of contents adequately describes the content on almost a page-by-page basis (with the backup and support of the subject index).

The first section includes a very impressive paper by Marc Schuckit reviewing his longitudinal research studies of children of alcoholics. The section overview and this first chapter set the tone for a well-organized, current, and very enjoyable scholarly reference. The remainder of the first section deals with issues relating to children of alcoholics such as neuropsychological factors, biochemical markers, neurophysiological factors, and genetics. It is not until the final section (pp. 287-344) that the most controversial aspects of the children of alcoholics movement are discussed.

Children of alcoholics represent a tremendously important

subject for clinicians. The children of alcoholics movement, like the self-help movement, the cocaine-is-dangerous movement, and other consumer-led medical revolutions, attempts to first bring to the attention of medical practitioners and researchers a concept that has been largely ignored. By identifying common characteristics and problems, the children of alcoholics have identified a syndrome and have challenged health professionals to study them and discover the consequences of living in an alcoholic family. They challenge all of us to help in the separation of nature and nurture by encouraging us to study children of alcoholics reared in nonalcoholic homes, adopted children of nonalcoholics in alcoholic homes, twins reared separately, and so on. Interestingly enough, we can see in this volume that clinicians are designing programs for prevention and education in the school and community and helping with treatment at the same time as the concept of children of alcoholics is being challenged by some.

It has been estimated that there are more than 20 million children of alcoholics over the age of 18 in the United States. Until very recently this fact has been ignored by medical researchers and clinicians. How children of alcoholics emerged as a consumer movement and did not evolve from Al-Anon or professional research or treatment is clearly described in the chapter by Brown. She shows us the emergence of the social movement of adult children of alcoholics, overnight with a clear identity, from beliefs and a body of literature based on personal accounts and clinical research. The movement is now more than 10 years old; the National Association of Children of Alcoholics was formed in 1983. Its proponents realize that academics question whether any generalizations about adult children of alcoholics can be made without prospective, or at least experimental, research. We psychiatrists are then perceived as reacting toward adult children of alcoholics the same way that "professionals" have reacted to Alcoholics Anonymous. Brown's chapter answers many questions that researchers and clinicians have about the adult children of alcoholics movement. The benefits of researchers and clinicians working together to do the necessary and important work of research and treatment evaluation are clear.

Dinwiddie and Reich jump right into the controversy on genetics and conclude that despite differences in research methodology most studies show the familial nature of alcoholism and that familial alcoholism is becoming more prevalent. The section on fetal alcohol syndrome is very well organized and comprehensive and could easily have been a book in itself. In five chapters this section provides the clinicians with nearly everything they need to know about this syndrome's medical and societal cost, neurobiology, clinical features, and prevention.

Similarly, the section on vulnerability to disease in the relatives of alcoholics and which diseases coexist with alcoholism is very useful. Of special interest for the researcher is the exhaustive chapter on vulnerability to cardiac disease, which has 318 references and six useful figures. This chapter is so well written that it is easy to understand cardiac effects even if you are not a cardiologist.

When compared with the remainder of the volume and the other sections, the section devoted to children of alcoholics provides information that has been available primarily through the general press. The authors are both comprehensive and critical of the methodology and conclusions of available studies and help us to organize what is really known, what is widely believed, and what programs are available in the schools and for treatment.

It would be difficult to imagine a finer academic reference

text on this subject. This book is surprisingly readable at the same time as it is encyclopedic in detail and organization.

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CLINICAL PRACTICE

Current Treatments of Obsessive-Compulsive Disorder, edited by Michele Tortora Pato, M.D., and Joseph Zohar, M.D. Washington, D.C., American Psychiatric Press, 1991, 191 pp., \$28.50.

This brief and helpful book is a superb example of nonobessional writing and organization about obsessive-compulsive disorder and related disorders. It is aimed, unabashedly, toward the clinician, not the academic, so those seeking a review of the basic science aspects of obsessive-compulsive disorder should seek elsewhere. Those who want a comprehensive, concise, well-written review of the diagnosis and treatment of obsessive-compulsive disorder cannot do better than this volume.

Recognized experts address the important clinical questions about obsessive-compulsive disorder. The style, conciseness, and organization are remarkably similar among the authors, showing an exemplary job of editing. Chapters on drug treatment cover clomipramine, fluoxetine, fluvoxamine, and several augmenting agents. Evidence derived from anecdotal reports is clearly distinguished from that derived from controlled studies. Do not expect critical reviews of the studies. The approach is more a listing of their salient features. Readers who want to delve deeper can seek out the plentiful references to the original studies and more comprehensive reviews.

Psychotherapy of obsessive-compulsive disorder receives equal attention to drug treatment. There are chapters on behavior therapy, family therapy, and multifamily group therapy. Behavior therapy and drug treatment have the benefit of support from methodologically sound research. The other techniques do not. I wish the authors stressed this difference more, although a careful reader learns this. Similarly, the disparity between the evidence for the efficacy of behavior therapy of compulsions (strong) and obsessions (weak) might have been more emphasized.

Each chapter about a treatment approach not only reviews the literature but presents specific clinical guidelines and case histories. The style is so concise as to be almost telegraphic, and the advice is apodictic, making treatment appear more straightforward than it is.

For me, the most interesting chapter was the one by Greenberg and Witztum on the treatment of obsessive-compulsive disorder in strictly religious patients, a topic that cries out for a more complete discussion. There are two problems here: 1) differentiating obsessive-compulsive disorder from normative religious practices and 2) how to talk to the patient whose religious views differ from the clinician's. In the usual case, the clinician is less strictly religious than the patient. Greenberg and Witztum offer reasonable advice about this.

In the last chapter, Hollander, much too briefly, considers the intriguing issue of whether drugs useful in obsessive-compulsive disorder might work in related problems, such as body dysmorphic disorder (e.g., "I can't stop thinking about how ugly my nose is."), trichotillomania (there are data from a controlled study supporting clomipramine treatment), and depersonalization (less convincing to me). Given the empirical

basis of our knowledge of drug treatments in psychiatry (i.e., capitalizing on unexpected findings rather than fully understanding mechanisms), most of our knowledge comes from taking an effective treatment and extending it to other disorders (e.g., imipramine, made to be an antipsychotic, was tried in depression). Since so much psychopathology can be thought of as unwanted repetitions, we should energetically test serotonergic drugs in all these possibly related disorders. At present we cannot say what are the limits of this treatment.

I recommend this book highly.

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Post-Traumatic Stress Disorder: A Clinician's Guide, by Kirtland C. Peterson, Maurice F. Prout, and Robert A. Schwartz. New York, Plenum, 1991, 225 pp., \$34.50.

Having read a review of this work, the reader is likely to ask why this book was not published 10 years ago. Seldom do we see a book that so well fulfills a need. A large number of observations and opinions have been reported on posttraumatic stress disorder (PTSD) in the last 10–15 years in a mushrooming fashion, and we needed a synthesis and a balanced summary. The authors completed exactly this task, presenting an ordered, exceptionally well-organized, and penetrating study of the syndrome of PTSD.

After a brief introductory history, which in itself is a very stimulating chapter (I am sorry that it is so short), the authors discuss the subject in four main divisions. The first part describes the primary and secondary symptoms clearly with proper emphasis on the relative importance of the symptoms from gross manifestations to finely perceptible nuances. The syndrome in the area of pediatric psychopathology is not forgotten. Reading over this first part alone, mental health professionals should feel more confident and secure to make their own diagnostic formulations and assessments.

The second part deals with theoretical considerations from all major viewpoints. Reference is made to important comments by early psychoanalytical writers, and the reader is led through behavioral theories, cognitive and psychosocial models, cybernetics, and ecosystem models. Psychodynamic formulations are predominant, however. I assume that this was the most difficult part of the book to write, and the authors should be commended for the maturity of their overview, the good balance maintained among the various propositions, and the high level of intellectual penetration to the core of the different theories concerning etiology and mechanism of action.

The third section of the book deals with formal assessment, with reference to the mental status examination and alignment with *DSM-III-R*. The fitness (and failures) of traditional psychological tests are well discussed, and differential diagnosis occupies a large part of this section. Social and legal aspects did not escape the attention of the authors; malingering and embellished exploitation of the syndrome for monetary advantage are well described without partiality in either direction. The difficult patient and special problems that cannot be easily fitted into existing diagnostic frames are described with sophistication plus some good suggestions hinted at here and there. Comorbidity is an outstanding example of such difficulties. It occurs quite frequently in actual practice, and the authors warn the reader that a certain bias on the examiner's part is practically unavoidable. I personally feel that the problem of comorbidity should have occupied a larger part of the

discussion because of its clinical frequency, particularly with regard to the Vietnam veteran.

The fourth and last section of the book is, of course, about therapy. Again, as in the preceding chapters, thoroughness is the outstanding virtue. The section is sufficient in details to teach or even to train clinicians to improve their therapeutic skills.

Modestly, the authors gave the subtitle of "A Clinician's Guide" to the book. This is correct, but the book is much more than this. It is a concise textbook. It is written without verbosity, yet it is not dry reading, always staying within the limits of the essentials. In spite of the fact that it is written by three different authors, the book has uniformity and fluency in its style. It is a most enjoyable reading. In the certainty that within a reasonable time a second edition will be forthcoming, I respectfully suggest that more attention be paid to the sexually and physically abused child. Child abuse is a subject, like PTSD itself, that is still under ongoing exploration. The abused child who responds with behavioral disaster to his or her abuse is often diagnosed as having conduct disorder instead of PTSD. I hope that the authors agree with this and give a little more space to the abused child in their second edition.

In summary, this book is wonderfully written in a most enjoyable, fluent style, bringing order and clarity to the subject of PTSD. It gives a great deal of useful hints to the practicing clinician and the academically oriented reader as well.

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Memory Disorders: Research and Clinical Practice, edited by Takehiko Yanagihara and Ronald C. Petersen. New York, Marcel Dekker, 1991, 503 pp., \$125.00.

As this book demonstrates, our usual ways of conceptualizing and assessing memory in clinical practice are outdated. Repeating a series of numbers forwards and backwards, recalling three words, describing what one ate for breakfast, and divulging one's birth date are supposed to assess immediate, short-term, recent, and long-term memory. But this division of memory is antiquated and in any case not assessed by the evaluation. If one always eats the same thing for breakfast is this a test of recent memory? Does one really remember when he or she was born? The model behind this viewpoint saw the brain as analogous to a pre-electronic office, with information flowing from desk to filing cabinets to back office to microfiche. Current views are more closely tied to neuroanatomy, not neurofantasy, and link different neuroanatomical structures with different memory functions. These functions include declarative or explicit memory (the only one tested by our current clinical examination) as well as procedural or implicit memory.

Declarative memory is that which one is aware of knowing. It can be divided into semantic memory for information that is not contextually bound (i.e., knowing your birth date) and episodic or autobiographical memory, actual recollections of yesterday's contextually bound memory. Implicit memory comprises a series of functions that one may not be aware of knowing, such as motor skill learning, procedural problem solving (i.e., doing the Tower of Hanoi problem), and different forms of priming (i.e., being able to recognize a word or shape more easily after previous exposure). Since these functions are subserved by different anatomical structures, individuals with disorders of declarative memory, which usually involve the hippocampus (e.g., Alzheimer's disease) or the dorsomedial

thalamic nucleus (e.g., Korsakoff's syndrome), may have intact implicit memory. For example, since the basal ganglia of amnesic individuals are intact they can acquire motor skill such as mirror writing without being aware that they have done so.

The first section of this book provides an excellent overview of these new models of memory function, their neuroanatomical and biochemical substrate, and the effect of drugs on these functions. Building on this information, the next section reviews methods to evaluate memory, including some simple clinical procedures such as the "three words and three shapes" test, which is a good candidate to replace much of our current memory assessment. The third section deals with memory dysfunction in neuropsychiatric disorders. Although informative, many of the clinical chapters do not make enough reference to the models presented earlier in the book. The primary reason for this is that a sufficient body of knowledge does not yet exist to accurately describe the full range of memory deficits and retained functions in many of the disorders. A striking exception to this is Craick's chapter on memory function in aging, which provides interesting findings on differential effects of normal aging on different types of memory, including declarative versus implicit memory. The final chapter deals with treatment and is less clinically useful than offering hints of future treatments.

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PSYCHOPATHOLOGY

Cognitive Bases of Mental Disorders: Annual Review of Psychopathology, vol. 1, edited by Peter A. Magaro. Newbury Park, Calif., Sage Publications, 1990, 307 pp., \$39.95; \$19.95 (paper).

This book launches a new annual review series, the first devoted to psychopathology. Each volume of the series will critically explore research into a specific element of psychopathology as it is expressed within conventional diagnostic groupings. Thus, this maiden volume is focused on cognition as it presents in obsessional illness, mania, antisocial personality, and so on. Later volumes will similarly treat such topics as personality, neurology, and social behavior.

This organizational strategy is a critical choice, and it is problematic. The editors argue that psychopathological signs and symptoms are not unique to specific diagnoses, that depression, for example, may appear with any of them. True enough. Psychopathological diagnoses are syndromes delimited by a mix of pathological signs and symptoms. Often one manifestation is necessarily present while many others may or may not be present. Depressed mood is a necessary feature of major depression, whereas it is often but not always present in obsessive-compulsive disorder. Sometimes, a specific sign cannot be accommodated within a syndrome; for example, delusions within panic disorder. Having accepted and worked with this basic logic for several decades, I found that focusing on only one psychopathological feature, in this instance cognition, is vexing and artificial without apparent compensating advantages. How is one to evaluate studies of cognition in depressed or manic persons without reference to mood or to associated phenomena such as diurnal variation? What do studies of memory in schizophrenia tell us if we do not simultaneously consider anxiety? The restricted perspective also

seems to undermine thinking about etiology. How can one formulate etiologic hypotheses concerning a defect in cognition that might be found across diverse diagnostic categories? Perhaps this is why "genetics" does not appear in the index and I found only passing mention of it in the text.

This book made me realize that there is little consensus about what is denoted by "psychopathology." Cognitive dysfunction in schizophrenia is defined by one author as "bizarre incoherence, inadequate or incomprehensible ideas." Can this mean that we ignore delusions when discussing cognition in schizophrenia? And indeed, delusions get no attention in that chapter and little anywhere else in this book. How are we to understand such an omission in a book that purports to deal with cognition in psychopathology?

Other problems with definition are illustrated in the long chapter (61 pages with 306 references) on "histrionic/over-conventional personality," a designation that appears more or less to fit with what was once called "grand hysteria." However, the criteria marshaled to delimit the entity are based on constructs such as "cognitive processing style" and "reflectivity-impulsivity personality style." Such psychometric abstractions are difficult to grasp, but, more fundamentally, what evidence links them to psychopathology? Where on the continuum of "reflectivity-impulsivity" is pathological, and what evidence establishes the implied association with disorder? What is the population base rate of pathological scores and what are the age- and sex-specific frequencies? What are the rates of type 1 and type 2 errors of classification? Such questions, the traditional meat of pathology, are not addressed.

A niche is surely available for the projected series of annual reviews of psychopathology. I hope it becomes a smashing success. However, I think that this volume is an unfortunate start. Psychiatrists will find little help with their diagnostic problems, and their insights into pathogenic mechanisms will be muddled, not strengthened.

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Person Schemas and Maladaptive Interpersonal Patterns, edited by Mardi J. Horowitz. Chicago, University of Chicago Press, 1991, 433 pp., \$34.95.

"Person schemas" are concepts in theories of psychology. They refer to mental structures of meaning that integrate knowledge about self and others, organize thoughts, feelings, and actions, and may operate consciously or unconsciously—which is to say they refer to just about everything that might interest a psychodynamically oriented clinician. Of course, there are other concepts in other psychological theories that refer to the same domain. Person schemas exist in the minds of psychological theorists just as these other concepts do. For the clinician, researcher, or student who is not irreversibly committed to one or another theory and its related concepts, the critical question is which are best or at least most useful for some purpose. Which concepts organize the data, suggest new questions, can be related to quantifiable, operationalizable, and reliable measures and instruments, generate interesting, testable, and falsifiable hypotheses, lead to creative and potentially therapeutic insights, suggest linkages to related fields of inquiry, have an aesthetic or intuitive elegance, and in general fulfill the criteria by which we evaluate concepts and theories in psychology?

This volume, the third from the Program on Conscious and Unconscious Process sponsored by the MacArthur Foundation, is edited by Mardi J. Horowitz, who directs the program. Dr. Horowitz writes or co-authors the introduction and six of the 17 chapters. I know of no work that explores the concept of person schemas more carefully and systematically, nor of any group more qualified to do so. The book consists of a collection of independent papers by experts who are at the cutting edge of an emerging interdisciplinary field. The papers vary in focus from detailed descriptions of how a specific instrument is employed to general discussions of the relationship between psychodynamic and cognitive models.

The volume is divided into four parts. The first explores the concept and the theory. The second introduces three specific methods, Horowitz' role-relationship models configuration, Lester Luborsky's core conflictual relationship theme, and Lorna Benjamin's structural analysis of social behavior (presented by Dianna Hartley). These methods are both described and applied to two case summaries, each of a professional man in his mid-30s with a "compulsive" personality who had been treated in Dr. Horowitz' clinic. The third part of the book compares the three methods, and the final part introduces a discussion of information processing models as potential schemas linking psychodynamic, cognitive, and neurobehavioral theories.

Each of the three methods that are discussed, explored, compared, and contrasted in the major part of the book is a strategy for reducing data and simplifying, codifying, and organizing clinical material as a step toward systematic research. The subject matter of the book focuses on the methods and the theories that generated those methods, not the psychological data or the investigation of behavior that these methods might allow. The discussion, therefore, will interest methodologists and researchers far more than clinicians or theorists. The ultimate test of any method is that it accomplishes some useful goal, but we are not yet up to that point; here we are only asking whether the method can be used at all and how it might compare with other methods. The casual reader will find condensed, systematic, and organized psychodynamic formulations that seem, as one might expect, somewhat abstract and formulaic and that contain few surprises. These studies demonstrate that these methods can be used; the next step—the new discoveries that might result from employing them—should be the exciting one.

The final section of the book is the most speculative. It discusses the relationship between psychodynamic theory and models derived from information processing, including an interesting discussion of the difference in the demands placed on such models by "simple" cognition or perception compared with the "quite novel combinations of conflicting, ambivalent or ambiguous conscious and unconscious thoughts, affects, expectations, drives and wishes about multiple people or events" (p. 341) implicit in psychodynamic theory.

Horowitz says, "Building a bridge between psychodynamic and cognitive science is possible, but it involves evolutionary change in both theories" (p. 413). He might have added that it is not yet clear what value such a bridge will have, how and whether it will enrich both theories, and whether the time is ripe to begin. He concludes by saying, "If that bridge can be built, it could lead to a much improved understanding of the cause and prevention of personality disorders, the enriched development of character, and the integration of the psychotherapies" (p. 423). This is the vision that drives the entire

project. Judging on the basis of the work discussed here, I think it remains an appealing but as yet unrealized potential.

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MELANIE KLEIN

Melanie Klein, vol. II: *The Ego and the Good Object, 1932–1960*, by Jean-Michel Petot; translated from the French by Christine Trollope. Madison, Conn., International Universities Press, 1991, 282 pp., \$40.00.

Melanie Klein, perhaps the most original of the early psychoanalysts after Freud, never achieved in the United States the importance she attained in Great Britain. One of the first child psychoanalysts, Mrs. Klein believed that "anxieties of a psychotic nature are in some measure part of normal infantile development," and she posited a crucial depressive position in the first year of life that was more than a stage; it was a basic structure of personality. Many American psychoanalysts dismissed her ideas because they seemed incompatible with what was known about cognitive and affective development in children. Mrs. Klein and Anna Freud were leaders of conflicting schools in England, but Anna Freud's ego psychology seemed to build a better bridge between academic psychology and psychoanalysis, and for this and for other reasons it dominated the scene in the United States. However, out of Klein's work would come object relations theory, a psychodynamic perspective that proved crucial to many psychotherapists. This was particularly the case for psychotherapists who attempted to treat psychotic and borderline patients.

As is now well recognized, Sigmund Freud's structural theory deconstructed the subjective sense of self and therefore sidetracked the possibility of a psychoanalytic conception of this crucial aspect of consciousness. Arguably, every important neo-Freudian from Sullivan to Horney to Erikson to Kohut to Lacan has had the task of reconstructing a phenomenologically meaningful psychoanalytic theory of the self. Klein's theory of object relations was the beginning of that enterprise. Feminists have now recognized Klein's importance as a theoretician and as a leading force in psychoanalysis.

Mrs. Klein's theorizing met opposition not just because she disagreed with Anna Freud and because her ideas seemed contrary to what was known about child development. As one of the first psychoanalysts to do play therapy, she imagined her way into the meaning of the play in interpretive narratives that seem to go far beyond her observations. Her paper "The Importance of Symbol Formation in the Development of the Ego" (1) is a classic both for its clinical brilliance and its overreaching. Mrs. Klein invented the concept of projective identification, and in her description of symbol formation in the child she seems at times to be using that mechanism. Despite her theoretical extravagances, Mrs. Klein opened a window into the aggressive and violent fantasies of the child, the good and the bad object, splitting, the transition from anxiety to obsession, the importance of envy, and other preoccupying emotional states of the young child.

Child psychiatrists who ignore Melanie Klein's writings deprive themselves of a unique insight into the anxious child's subjective experience. If Sigmund Freud's work tore the veil of repression from infantile sexuality, Mrs. Klein exposed the violent passions and the related terrors of that supposed age of happy innocence.

Petot's volume, the second he has devoted to Mrs. Klein, deals with her writings during the years she was elaborating her theories and establishing the "Kleinian school" in England. Mrs. Klein's "discovery of the depressive position in 1934" launched this period of theory building. Petot writes in French, but the translation by Christine Trollope captures Petot's underlying thesis. He insists that Mrs. Klein has actually *discovered* something which is really there and that her work has both "heuristic value and objective validity." He claims that Klein's theories are fully compatible with those of Piaget and what is known empirically about child development. The study of infants has certainly pushed back the frontiers of psychological development, but whether Klein's speculations can be confirmed is another matter. For example, as Petot recognizes, many American psychoanalysts have found in the "separation" experience enough to make Klein's theories superfluous. Furthermore, "separation" and its effects can be studied in other species. The depressive position, with its symbols, splitting, mechanism, etc., may be compatible with empirical data but may not be confirmable except at the level of human empathy.

Petot's book is written with the painstaking precision of a philosopher, with the clinical understanding of a psychoanalyst, and with the empirical perspective of a developmental psychologist. Trained in all these disciplines, Petot has brought them together in this exegesis of Mrs. Klein's theories. Many psychoanalysts have attempted to explain Melanie Klein or to offer their own versions of her work. None has produced a clearer exposition. Even Mrs. Klein might agree that of all her students, Petot has the clearest sense of her ideas. Unfortunately, his impeccable scholarship will be impenetrable to those who do not already "speak" Kleinian. For those who still need an introduction to Mrs. Klein's work, the collection assembled by Juliet Mitchell (1) is the place to go before you try to wade through the deep going of Petot's very important contribution to Klein scholarship.

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SELF PSYCHOLOGY

Progress in Self Psychology, vol. 6: The Realities of Transference, edited by Arnold Goldberg. Hillsdale, N.J., Analytic Press, 1990, 263 pp., \$32.50.

Such diverse subjects as empathy, the working through of "selfobject" transferences, selfobjects of the second half of life, the origins of ambition, addictive personalities, AIDS patients, Vincent van Gogh, and the application of evolutionary biology to psychoanalysis are examined in this volume. What is the unifying thread? Kohut clearly hoped that his self psychology would advance a new humanism in psychoanalysis and expand into a general psychology. The editor of this book, the sixth volume in a series devoted to progress in self psychology, strives for that goal by inviting contributors to broaden the perspective of self psychology by applying it to the arts, biology, and the somatopsychic conditions.

The book is divided into four major sections: Progress in

the Theory of Self Psychology, Progress in Development, Progress in the Approach to Psychopathology, and Progress in the Application of Self Psychology. The first section consists of half of the 14 papers in the book and deals with the evolving theory of self psychology. Here, Stolorow discusses Lichtenberg's paper "Rethinking the Scope of the Patient's Transference and the Therapists' Counterresponsiveness" and Leider's "Transference: Truth and Consequences," and Lachmann comments on Anna Ornstein's "Selfobject Transferences and the Process of Working Through." Such an arrangement provides for continuity and perspective in the section. The articles under discussion are well-written and offer interesting perspectives. The reader gets the flavor of participating in a 1-day workshop of the local psychoanalytic society, complete with a discussion of the papers. Basch and Meares round out the section on theory by sharing their thoughts on empathic understanding and the role of material objects in the development of the self, respectively.

The section on progress in development is disappointingly brief—only one paper by Galatzer-Levy and Cohler, who write about selfobjects in the second half of life. It maintains the growing emphasis on viewing development as a continuous life process with epochs and critical events. This chapter is clinically refreshing and lucid while weaving in the tenets of self psychology in a convincing manner.

The three papers in the section on progress in the approach to psychopathology deal with popular and relevant subjects: the ambitions of women, addictions, and the psychodynamic consequences of AIDS. Leib presents a very readable, current self psychology perspective of the struggles women face in their ambitions related to motherhood and family, work, and making an impact on their environment. Cohen and Abramowitz share their experience and understanding gained from

working with AIDS patients. They give a highly informative and sensitive account of the devastating impact of AIDS on the self and suggest helpful therapeutic approaches.

In the final section on progress in the application of self psychology, the three papers examine the therapist as muse, identify and expand on selfobject factors in Vincent van Gogh's creativity, and suggest clues from evolutionary biology to help explain the resistance to self psychology. Of the three papers I found Baker's "Vincent van Gogh: Selfobject Factors in Motivating, Facilitating, and Inhibiting Creativity" the most intriguing. Baker has researched his subject well and draws on his impressive knowledge of art and culture as well as psychoanalysis to offer the reader an attention capturing and plausible narrative of the significant object relationships in Vincent van Gogh's tortured existence and their impact on his creativity.

Does *The Realities of Transference* meet Kohut's exacting standards and satisfy his vision of extending the psychology of the self to a general psychology? The objectives for the papers were attained insofar as they embrace a wide scope of topics and persistently interpret the phenomena from the self psychology perspective. Among the potpourri of papers there was some variation in the academic depth and organization, and perhaps the reader will be drawn more to one section than another. Most annoying was the surprisingly poor copy editing; spelling errors abounded, sentences were printed twice, and syntax was violated. Overall, however, both novitiates and early devotees of self psychology are certain to find several chapters of interest that illuminate the ongoing progress in self psychology.

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Reprints of Book Forum reviews are not available.

Letters to the Editor

Recovery From Protracted Depression in Old Age

SIR: Recovery from very long episodes of depression has been described in younger (1, 2) but not older patients. Thus, I report the case of an 80-year-old man who recovered from a depressive episode lasting 7 years.

Mr. A was a 74-year-old businessman who presented with a 1-year history of depression, anxiety, decreased concentration, anorexia, initial and middle insomnia, anhedonia, and loss of interest in and withdrawal from previous activities. There was no past personal history of affective disorder, although he drank 6 ounces of scotch per day most of his adult life. His physical health and cognitive function were excellent.

With encouragement, Mr. A stopped drinking. Despite receiving antidepressant medication and a course of ECT he remained depressed for 6 more years. Antidepressant medication included successive trials of imipramine, trimipramine, nortriptyline, trazadone, and phenelzine, alone or in combination with lithium carbonate, at maximum tolerated doses, for 4 to 6 months. Finally, 7 years after he first became ill, Mr. A recovered completely. Three years later, at age 83, he continued to enjoy life to the fullest and resumed all of his activities.

It is possible that the patient's recovery was related to antidepressant treatment but more likely that it was related to the natural course of his illness. In either case, the persistence of treatment was important to the patient in coping with the hopelessness induced by his prolonged illness.

Follow-up studies of younger patients with protracted depression have reported rates of recovery from this condition and prognostic factors (3, 4). Similar studies of older patients are needed. In the meantime, this case report provides some hope to therapists, patients, and their families, that recovery in old age may come even after very long periods of illness.

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Use of Cocaine to Prevent Opiate Withdrawal

SIR: We have previously reported that cocaine-dependent opiate addicts have less severe naloxone-precipitated withdrawal

than opiate addicts not dependent on cocaine (1) and that, in morphine-dependent rats, acute pretreatment with cocaine attenuates the severity of naloxone-precipitated withdrawal (2). However, the purposeful use of cocaine to prevent opiate withdrawal has not been previously described. The following patient reported using cocaine to minimize his opiate withdrawal symptoms.

Mr. A, a 32-year-old man dually addicted to cocaine and heroin, was admitted to the inpatient unit for a research protocol, during which he would be administered cocaine. He reported preferentially injecting the combination of a \$20 bag of heroin with a \$5 dollar bag of cocaine. He claimed that he added the cocaine, on the advice of his dealer, because cocaine postponed his opiate withdrawal symptoms (rhinorrhea and stomach cramps) for 1 hour or longer.

Mr. A claimed only minor subjective effects from a \$5 bag of cocaine. He claimed that he did not like using higher doses of cocaine or using cocaine alone. He was administered cocaine, 2 mg/kg intranasally, in combination with methadone, as part of a research protocol. He reported that this higher cocaine dose was anxiogenic and generally unpleasant. At the end of the protocol, Mr. A was referred to methadone maintenance. He reported that he had not used cocaine during his first 4 months on methadone maintenance.

Mr. A's cocaine use stopped when his opiate dependence was treated. A subset of addicts who use low amounts of cocaine cease cocaine use after entering methadone treatment (3). This patient's "prophylactic" use of low doses of cocaine distinguished him from the majority of dually addicted patients we have interviewed. Most dually addicted patients report having experienced opiate withdrawal after cocaine use and report no relief of opiate withdrawal by using cocaine (submitted abstract of S. Stine and S. Satel). Although an addict's claim that he uses cocaine to treat opiate withdrawal may not reflect a true cause-and-effect relationship, it is relevant information for designing a treatment plan.

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Oral Versus Intravenous Caffeine Augmentation of ECT

SIR: R.J. Ancill, M.D., and W. Carlyle, M.D. (1), recently reported the use of oral caffeine for augmentation of seizures during ECT when intravenous sodium caffeine benzoate is unavailable. They used doses of 300 to 1000 mg, 1 hour before treatment and reported that geriatric patients responded with longer seizures without increased anxiety or adverse hemodynamic effects.

Several augmentation techniques have now been described for eliciting adequate seizures in patients who develop a high seizure threshold during a course of ECT. These include the use of intravenous caffeine (2) and the use of oral theophylline (3). While oral caffeine may be an adequate substitute when the intravenous preparation is unavailable, we believe that the intravenous route is probably preferable. Intravenous caffeine administration allows titration to the minimal effective dose for each treatment. We initiate intravenous caffeine at the ECT session when we are first presented with an inadequate seizure at maximal stimulation. If an adequate seizure is not elicited, caffeine can be added intravenously while anesthesia is continued. We then restimulate the patient 5 minutes after administration of the caffeine. Such intervention would not be possible with the oral technique described by Drs. Ancill and Carlyle. The rationale for utilizing the smallest possible dose relates to the potential hemodynamic and dysrhythmogenic complications of caffeine treatment described, respectively, by Acevedo and Smith (4) and by us (5). Like Kellner and Batterson (6) we find that dosages lower than those originally recommended can prolong seizure length. A one-half ampule of sodium caffeine benzoate (125 mg active caffeine) is often effective. Given the slow elimination of caffeine, with a half life of 140–270 minutes after intravenous infusion (4), and a (presumably) longer effect after oral intake, the use of the most rapid intervention would be superior in geriatric or medically compromised patients.

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Dr. Ancill and Dr. Carlyle Reply

SIR: We welcome the comments of Dr. Jaffe and Dr. Dubin concerning oral versus intravenous caffeine augmentation of ECT. We certainly support the use of augmentation techniques, especially in patients who have developed a high seizure threshold or for whom the standard settings produce an unacceptable level of confusion. As we pointed out in our original letter, the option of using an intravenous regime is

not available to us and we wished to share our experience with the oral preparation of caffeine in order to advise our colleagues of this possibility.

Whether or not, as Drs. Jaffe and Dubin point out, intravenous caffeine does have advantages should be determined by controlled studies. However, we can confirm that with our increasing clinical experience we can report no significant side effects from utilizing the oral route.

Of particular interest to us is not only the ability to reduce the seizure threshold in patients who fail to have an adequate seizure but also to reduce the side effects, especially confusion, in geriatric patients with cognitive impairment who have significant depressive syndromes that will respond to ECT.

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Retinopathy and Bright Light Therapy

SIR: Dr. Wendy Vanselow and colleagues (1) raise the concern that light therapy of 2000 lux may damage the retina in susceptible human eyes and exacerbate existing retinopathy. They recommended mandatory ophthalmological screening of all patients with seasonal affective disorder.

We believe that their concerns and recommendations are unwarranted for the following reasons.

First, even in the case of the patient with serious retinopathy described by Dr. Vanselow and colleagues, suggestions that light therapy would be deleterious are purely speculative. Although staring directly into the sun (with a luminance of approximately 1.7×10^5 cd/cm²) can induce serious retinopathy (2, pp. 43–68), there is no evidence that such retinopathy can be induced by the levels of light used in light therapy (0.7 cd/cm²). Even in the condition where the potential for bright skylight (100,000 lux or 3 cd/cm²) damage to the retina has been most widely discussed, namely age-related macular degeneration, this putative causal relationship remains highly controversial (2, pp. 89–124).

Second, light therapy levels, even at 10,000 lux, are not very bright compared to bright skylight (approximately 100,000 lux). Light therapy at 2000 lux is comparable to looking at the sky during sunsets and sunrises. Although rodent retinal photoreceptors can be damaged at intensities much less than 2000 lux (2, pp. 69–88), in primates such damage has been demonstrated only at 10,800 lux with the eye dilated for 12 hours of continuous exposure (3). Exposing a monkey's undilated eye at this intensity 12 hours per day for 4 weeks does not produce photoreceptor damage (4). We have estimated that, in a worst-case analysis, over 6,400 half-hour sessions of light therapy at 10,800 lux (0.7 cd/cm²) would be required to induce threshold photoreceptor damage in the human retina. That is equivalent to approximately 73 winters of daily light therapy (M. Waxler et al., unpublished manuscript).

Third, there is no evidence that ophthalmological examination can detect prior light-induced photoreceptor damage. Thus, there is almost no benefit to be gained from ophthalmological screening in all cases. Furthermore, the extremely bright light of the ophthalmoscope (200 cd/cm²) has the potential for phototoxic effects in lengthy ophthalmological examinations and has itself been a focus of concern (5).

Although there is no evidence that light therapy exacerbates human retinopathy, there is some theoretical concern. Therefore, we recommend taking a careful ophthalmological history and consulting with an ophthalmologist or optometrist

if deemed necessary. To err on the side of caution, we would recommend not administering light therapy to patients with aphakic eyes and those with actively degenerating retinal disorders, such as diabetic retinopathy, retinitis pigmentosa, and age-related macular degeneration. In addition, we recommend excluding patients who are being treated with hematoporphyrin or similar highly light-sensitive compounds.

We have previously commented on the potentially harmful effects to the eye of light sources containing UV light (6) and recommend screening out UV rays during light therapy unless UV rays are found to be important for an antidepressant effect, an unresolved issue at present.

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Dr. Vanselow and Associates Reply

SIR: In dismissing the advisability of pretreatment eye checks for light therapy, Dr. Waxler and colleagues fail to address two important matters raised in our initial letter.

First, considerable variability in susceptibility to retinal phototoxicity is described, and particularly light-induced damage may exist in already diseased or damaged retinas (1). Recent reports implicate ambient light exposure as contributing to the process of age-related macular degeneration (2), and the morphology of that condition closely resembled the changes in our patient's left eye.

Second, considerable medicolegal importance may be given to the detection of preexisting retinal lesions in patients about to undergo treatment that is arguably retinotoxic.

The comment by Dr. Waxler and colleagues that "almost no benefit is to be gained from ophthalmological screening in all cases" is contradictory to their own recommendation to take "a careful ophthalmological history and consulting with an ophthalmologist . . . if deemed necessary." Experience has shown that many patients are unaware of preexisting eye damage, as was illustrated by our case history.

In view of the relative ease of obtaining a pretreatment ophthalmological examination it would seem foolhardy to omit

one when this could be considered essential to informed consent.

Furthermore, by undergoing a comprehensive eye check there may be the added benefit of reinforcing the need to adhere to strict guidelines for use of the light box. It is not difficult to imagine how a therapy that is increasingly available for use in the home without direct supervision could be misused by the person not only for whom it was intended but by other household members.

We would, therefore, conclude that a minimum standard of care for recipients of phototherapy should include ophthalmological screening and surveillance.

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DR. STUART ARMSTRONG
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Comorbidity of Personality Disorders

SIR: The recent article on patterns of comorbidity of personality disorders by John M. Oldham, M.D., and associates (1), exemplifies the arduous work needed if we are to better understand their fundamental features. As have others, the investigators found that patients often met criteria for more than one personality disorder, leading to the suggestion that a two-level system be used on axis II. Patients meeting criteria for two or fewer disorders might be viewed as having a "focal" personality disorder, while those with more than two disorders would receive a diagnosis of "extensive" personality disorder, including a description of the predominant characteristics present. While this suggestion has merit, we are concerned that the term extensive could be taken to mean that the patient has a more severe condition, or one with a poorer prognosis, than does one with a "focal" disorder, as is implied when one speaks of focal versus extensive lesions in medicine. This may not be the case, as a patient with one or two disorders may show impairment as severe as one with several disorders. A less potentially pejorative term, such as diverse personality disorder, might better describe those cases wherein patients meet criteria for three or more disorders. Clearly the high degree of overlap among categories and the modest agreement between the two interviews used indicates the need for further research in this area.

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Dr. Oldham and Dr. Skodol Reply

SIR: We received the letter from Dr. O'Boyle and Dr. Holzer and appreciate their recognition of the complexity of comorbidity studies of personality disorders. They express concern regarding our suggestion to adopt a convention that a patient with three or more personality disorders be diagnosed as having "extensive personality disorder," followed by a list of characteristics using *DSM-III-R* diagnostic terms. Their concern that "extensive" might erroneously imply a measure of severity is well taken. Certainly, there are patients with selected single personality disorder diagnoses or with only two who are more ill than patients with three or more less disabling diagnoses. In our experience, however, numbers of personality disorder diagnoses in a given patient are frequently correlated with severity of psychopathology and impairment in functioning. An alternative word, such as "diverse," would accomplish our purpose and would be entirely acceptable. Still needed are studies that address the applicability of a hierarchy among the personality disorders for cases meeting criteria for multiple disorders. Nonetheless, we are grateful to Drs. O'Boyle and Holzer for their suggestion.

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Obesity and Multiple Personality Disorder

SIR: Donald W. Black, M.D., and associates (1) sought to determine the association between mental disorder and morbid obesity in 88 bariatric clinic patients. They reported an empiric correlation between morbid obesity and anxiety disorders (most prominently posttraumatic stress disorder [PTSD]), mood disorders, bulimia, and tobacco dependence but did not screen for dissociative disorders.

Once thought to be extremely rare, the dissociative disorders have recently come to be seen as a major category of psychopathology affecting up to 10% of the population (2). The patient sample reported by Dr. Black and associates may have been at even higher risk for dissociative disorders because they were predominantly female (3), had low socioeconomic status, and had high rates of PTSD and eating disorders (4).

Surgical treatment of obesity in a patient with multiple personality disorder might be contraindicated if it were found that the obesity was the result of the covert actions of one "personality." A screen for dissociative disorders would be very helpful to those doing treatment planning and could be accomplished using such measures as the Dissociative Experiences Scale and the Dissociative Disorder Interview Schedule (5).

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HOWARD WETSMAN, M.D.
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SIR: Morbid obesity is associated with significant emotional distress. Dr. Black and colleagues demonstrated this finding in the preoperative assessment of gastric stapling patients, noting high lifetime rates for mood disorder, anxiety disorder, bulimia, and personality disorder. However, caution should be exercised in inferring specific psychopathology in the morbidly obese, and the authors rightly point to the need for longitudinal study to assess fully the psychosocial outcome of vertical banded gastroplasty.

We conducted a prospective evaluation of gastric stapling patients (1) with similar sample characteristics (age, sex, race, socioeconomic status) using comprehensive assessment measures of clinical interview, *DSM-III* axis I and II diagnoses, locus of control, eating disorder profile, and measures of lifestyle, sexual function, and interpersonal relationship. Patients were examined preoperatively and postoperatively after a mean period of 13.6 months at which point the mean loss of weight was 46.4 kg. At baseline, measures of anxiety, dysthymia, and somatic concern were noted to be high. However, a significant reduction was noted in the postsurgical period. In addition, many aspects of personality showed some change, with reduction of schizoid, avoidant, and passive aggressive traits and, to a lesser degree, some increase in histrionic and narcissistic characteristics. Improvement in interpersonal relationships, sexual function, socialization, and self-perception was noted. The Eating Disorder Inventory (2) demonstrated the large measure of body dissatisfaction in the morbidly obese even exceeding the levels known for anorexia nervosa. Significant improvement was noted after surgery. Of importance was the absence of major psychiatric illness in patients before or after surgery. In general, these findings compliment our previous study of gastric surgery patients (3).

Although distress was prominent in the morbidly obese, in contrast to Dr. Black and associates, we did not find psychiatric illness. Moreover, even axis II pathology or personality disorder assessed by the Millon Clinical Multiaxial Inventory (4) was not prominent. However, change in personality profiles was noted postsurgically, suggesting a state-dependent rather than trait condition linked to morbid obesity. Obviously the differences in the various studies may depend to some extent on methodological issues such as the type of instrument used to measure psychiatric illness, covariation between disorders, etc. However, in light of our data, specific psychopathology—particularly personality disorder—attributed to the morbidly obese remains unproven.

It will be interesting to see the results from Dr. Black and colleagues of the patients after gastroplasty, both to assess outcome and elucidate relevant psychiatric variables. In future studies it will be important to broaden outcome measures to include general physical health and quality of life.

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DR. PRAFUL C. CHANDARANA
DR. PATRICK CONLON
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Dr. Black Replies

SIR: Dr. Wetsman has made several interesting and useful comments about the prevalence of dissociative disorders in morbid obesity. The Diagnostic Interview Schedule (DIS) does not include dissociative disorders and to screen for this would require using another instrument, such as one of those that he recommends. As he notes, preliminary data suggest that morbidly obese subjects are prone to developing dissociative disorders. I doubt that dissociative disorders are as prevalent as Dr. Wetsman believes, but I look forward to seeing additional data on this group of patients to confirm or refute these associations.

I thank Drs. Chandarana and Conlon for bringing their work to our attention. In their study of gastroplasty patients, they failed to find psychiatric illness and noted that "even axis II pathology or personality disorder" was not prominent. Despite our data and that of others, they believe the association of psychiatric illness and morbid obesity remains unproven. We beg to differ. As noted in our article, a comprehensive survey of the literature published since 1960 pertaining to psychiatric diagnosis in morbidly obese subjects shows a strong link between morbid obesity and various mental illnesses, particularly depression and personality disorders.

Our study is one of the first to use structured interviews to assess both axis I and axis II disorders in morbidly obese persons and to provide a comparison group. Unless one dismisses outright the value of these assessments (the DIS and the Structured Interview for DSM-III Personality Disorder), both adequately studied for reliability and validity, one must assume that the findings have value. In fact, morbidly obese persons have substantial axis I and axis II pathology that should be taken into account by their caregivers. I suspect that the findings of Drs. Chandarana and Conlon differ from ours because they did not use structured interviews but relied on self-report instruments not designed to generate diagnoses. We, too, have data from self-report instruments that we will publish in the future, along with data collected 6 months and 1 year after gastroplasty to test the association between psychopathology assessed at intake and weight loss in follow-up.

DONALD W. BLACK, M.D.
Iowa City, Iowa

Caloric Requirements for Weight Maintenance: A British Viewpoint

SIR: While agreeing with Theodore E. Weltzin, M.D., and associates (1), that "elevated caloric requirements . . . may particularly contribute to relapse in anorexic patients," I am disquieted to read that physical activity has not been included as an independent variable.

Many of the anorexic patients admitted to our eating disorders unit use exercise as a method of weight control in addition to dietary restriction. In the experimental condition de-

scribed by Dr. Weltzin and colleagues, where food intake is measured with such accuracy, an increase in exercise by an anorexic patient could be anticipated. Discharge from the restriction of a hospital environment may also precipitate an increase in physical activity in an anorexic patient. A long-term, weight-stable anorexic woman is less likely to exhibit the compulsion to increase her activity level.

The variation in physical activity is accounted for in the estimated energy requirements in the United Kingdom (2). The formula applied is that the daily energy expenditure is a multiple of the basal metabolic rate and the physical activity level. For example, the estimated energy requirement for an inactive, 55 kg, 20-year-old woman is 7.6 MJ/day (1828 kcal/day) and for a very active, but otherwise similar subject 12 MJ/day (2887 kcal/day): a discrepancy of 1059 kcal/day. Hence the contention that exercise must be considered when estimating caloric requirements.

A second point of interest is that the recommended weight table in the United Kingdom is that recommended by Passmore and Eastwood (3, pp. 44, 55, 518, 521). When Metropolitan Life Insurance Co. tables (4) are quoted (5) they are listed as the 1983 version, not the 1959 version as described in the article by Dr. Weltzin and colleagues.

It would be interesting to know the rationale for excluding physical exercise from the calculation for caloric requirement and why weight tables that in the United Kingdom are considered outmoded were used.

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SHEILA H. MERRIMAN, S.R.D.
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Dr. Weltzin and Associates Reply

SIR: We agree that increased physical activity may contribute to increased caloric needs and relapse in women with anorexia nervosa. In fact, in an earlier article, one of us (1) reported that physical activity, as measured by counts of movement using an acceleration-sensitive device with a solid state memory worn on the waist, was positively correlated with calories required to gain weight in anorexic subjects. Nevertheless, we did not measure physical activity in this study because we know of no method that can accurately measure the amount of energy used in physical activity in a free living environment.

The aim of this study was to measure caloric needs necessary for weight maintenance in anorexia and bulimia nervosa patients by measuring actual caloric intake. While a formula can be used to estimate the amount that physical activity contributes to daily energy expenditure, using such a formula may

be problematic. That is because other factors may contribute to increased caloric requirements in short-term recovered anorexic women; for example, increased resting metabolic rate or increased thermogenic response to ingested food (2). Overall, factors that contribute to increased caloric needs in short-term weight-recovered anorexic women remain to be characterized.

Insofar as we know, the choice of which tables to use to compare eating disorder patients to the general population is relatively arbitrary. To our knowledge no study has characterized an "ideal body weight" in anorexia. Body weights for similar frames are several kilograms greater in the 1983 tables as compared to the 1959 tables. Our clinical experience is that getting anorexic patients to gain to between 95% and 100% of the 1959 tables is adequate for reversing malnutrition. No data suggest that having anorexic patients attain the normative mean of the higher 1983 Metropolitan Life Tables would make any meaningful difference in terms of physiological improvement, such as normalization of reproductive function. In fact, adopting the 1983 tables could potentially increase length of treatments and increase resistance to suggested target weights in eating disorder patients.

We do not disagree with the use of either the 1983 or 1959 tables. We are currently conducting studies aimed at better understanding the relationship between normalization of body weight and physiological function, such as return of reproductive function, in women with eating disorders. A better understanding of the relationship between body weight and treatment response would significantly help clinicians in recommending maintenance weight for women with anorexia nervosa.

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Treatment of Neuroleptic-Resistant Mania and Schizoaffective Disorders

SIR: E.S. Garza-Treviño, M.D., and associates (1) have reported that verapamil is as effective as lithium in the treatment of acute mania. They mention that during their study, seven out of the 12 patients treated with verapamil received a combination of haloperidol and lorazepam to control excessive agitation.

Over the past several years I have investigated the effects of a calcium channel antagonist, nifedipine, in neuroleptic-resistant schizoaffective patients and in manic patients who were slow to respond to neuroleptic medication. I chose nifedipine because it has been reported to have depressant effects in normal persons (2). I have so far studied seven patients, all of whom have been treated with high doses of several neuroleptics with no improvement after at least 10 days of treatment (Brief Psychiatric Rating Scale [BPRS] scores still remaining above 60). The dose of nifedipine used was 120 mg/day, given

orally. Two of the seven patients rapidly and dramatically improved after nifedipine administration (in 48 hours) and three consistently improved, but more slowly. Nifedipine had no obvious effects in the last two patients. Nifedipine was withdrawn in all the patients before they were discharged. Two of the patients who had responded favorably (one of them in less than 48 hours) to the neuroleptic-nifedipine combination relapsed 12 and 18 months, respectively, after discharge. For 3 days following readmission, they were given nifedipine without neuroleptics, and this treatment alone had no effect.

This short study shows that the effects of neuroleptics in some patients can be enhanced, sometimes dramatically, by the addition of a calcium channel antagonist. Nifedipine alone does not appear to have rapid antimanic effects. Although the procedure I used is quite different from that of Dr. Garza-Treviño and associates, I suggest that the addition of haloperidol in their verapamil-treated patients may have been more than an adjunct to control the behavior. Haloperidol could have interacted with verapamil and resulted in the two drugs mutually potentiating each other. I do not think this reduces the interest of the work of Dr. Garza-Treviño and associates, but I think that discussions about the antimanic effects of calcium channel inhibitors should clearly differentiate the proper effects of these drugs from those of neuroleptics, since animal studies show that their action on locomotor activity can be either totally different (3) or related through an interaction on dopamine receptors (4).

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RENAUD DE BEAUREPAIRE, M.D., PH.D.
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Dr. Garza-Treviño and Associates Reply

SIR: Dr. de Beaurepaire has raised the possibility of a pharmacological synergism between haloperidol and verapamil having affected the treatment responses in our study comparing verapamil versus lithium in a randomized sample of 20 bipolar patients in the acute phase of a tic episode. This is an interesting idea which possibly deserves further investigation. However, it is important to emphasize that only three of the 12 verapamil-treated patients received most of the adjunctive medications in our study. (Five of these patients received no adjunctive medications, three received one dose, and one each received three, five, eight, and nine doses. Of the eight lithium-treated patients, three received no adjunctive medications, two received one dose, and three received three doses.) Those three patients receiving the most doses of adjunctive medications also scored higher on the Petterson Mania Scale than the rest, and their adjusted analysis of covariance (ANCOVA) posttreatment values changed less than the average. For those reasons, their scores

did not significantly affect the results of our study (nonsignificant difference between treatments). The same conclusion would have followed if those three patients in the verapamil group had been left out of the statistical analysis. The pretreatment (unadjusted) means of the BPRS were 40 for verapamil and 33 for lithium, and the Petterson Mania Scale scores also showed that, by chance, the verapamil group was more severely ill. Higher baseline scores provide greater possibility for improvement and can contribute to an apparent treatment effect (1, 2). Consequently, the measures had to be adjusted by ANCOVA. Following statistical adjustment, we noted a slight trend to favor lithium in our data, partly due to the fact that the three verapamil patients who received the most frequent adjunctive haloperidol evidenced relatively small covariance-adjusted change. However, the overlap between the groups was so great that larger samples would be required to demonstrate a statistically significant difference. Using appropriate formulas, it was determined that a sample size of 40 patients per group would be required to achieve a power of 0.80 for a treatment effect as great as that observed in this study. In that light, the observation of Dr. de Beaurepaire based on six patients is interesting, but hardly conclusive.

Nevertheless, we believe that Dr. de Beaurepaire has added to previous evidence (3) that other calcium channel blockers (e.g., nifedipine) have antimanic effects, though they act synergistically with other conventional treatments for mania. This should provide further stimulus to investigate whether there is indeed a role for calcium channel antagonists in the treatment of the lithium-resistant patient population. Further studies should clarify the issues of efficacy and possible synergistic effects.

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JOHN E. OVERALL, PH.D.

LEO E. HOLLISTER, M.D.

Houston, Tex.

Automobile Driving by Psychiatric Patients

SIR: We read with great interest the letter by Leo E. Hollister, M.D. (1), concerning driving by psychiatric patients. Dr. Hollister points out that textbooks of psychiatry lack any guidelines concerning traffic accidents related to psychiatric impairment. However, we managed to find many articles that addressed the question of accident proneness among psychiatric patients, one of them in the *Journal* (2). Psychiatric patients with personality disorders and paranoid disorders were reported to be at risk of having traffic accidents (2, 3).

Edlund et al. (4) found a greater rate of traffic accident involvement among 103 schizophrenic patients compared to a control group. They reported that schizophrenic patients drive substantially less than controls and thus may be at

greater risk of motor vehicle accidents per miles driven than age-matched controls. Schlosberg (5) reported equal rates of traffic violations and accidents in a group of schizophrenic patients and a control group, but he did not take into consideration the difference in miles traveled in the two study groups.

Many methodological problems arise in the field of accident proneness research. We must take into account issues such as diagnosis, drug therapy, recent stress, exposure, etc. These issues render accident proneness research an intriguing challenge for public health officials and explain why no conclusion has yet been drawn.

We agree with Dr. Hollister that this issue cannot any longer be evaded. However, the patient and the patient's family should not be responsible for this matter, even if they are the first to recognize the driving limitations. Giley et al. (6) reported that many patients with dementia do continue to drive, even when impaired. Thus, physicians in our opinion are responsible for the well-being of their patients and the welfare of society. In this instance the rights of the society should prevail over the rights of the individual. We conclude that psychiatrists and other physicians should take a more active role in the battle against traffic accidents. Education, research, and referral to driving fitness assessment with the medical and licensing authorities should all be a part of a greater involvement of the medical profession in order to combat traffic accidents.

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DR. IANCU IULIAN

DR. WIENER ADA

Tel Aviv, Israel

Dr. Hollister Replies

SIR: Is my face red? How could I have missed the three additional references pertinent to driving by psychiatric patients which are cited by Drs. Iulian and Ada? Probably no one doubts that, as a group, psychiatric patients of all kinds would have a higher rate of automobile accidents than unaffected persons. The problem comes in making a determination in an individual case. I did not mean to imply that the patients' opinions should be sought but rather those of the persons closest to them. Relatives and friends might be aware of problems which could escape detection during the usual psychiatric visit. As most psychiatric patients drive with insurance protection furnished by relatives or friends, the latter should be highly concerned about the patient's fitness to drive. The psychiatrist can make a better judgment about the issue of driving if these additional sources of information are consulted. They

might also be the strongest allies in enforcing any recommended restriction on driving.

LEO E. HOLLISTER, M.D.
Houston, Tex.

Steroid Use and Aggression

SIR: We read with great interest the case reported by J. Thomas Dalby, Ph.D. (1), of a sustained aggressive and antisocial reaction in a 20-year-old man after "brief exposure to a low dose" of the anabolic steroid Equipoise. However, based upon the subject's self-administration schedule and the pharmacologic profile of Equipoise, he was not exposed to a "low" dose nor was this exposure "transient," which brings into question the author's interpretation of the case.

Equipoise (boldenone undecyclate) is an injectable veterinary anabolic agent marketed primarily for use in the treatment of debilitation in horses. Despite its status as a veterinary drug, we have found that it is commonly diverted to the steroid "underground market" for human use. The compound is a depot anabolic agent formulated in sesame oil. It has a rapid onset of action, yet provides relatively stable high drug concentrations over a prolonged time period. The package insert from the manufacturer notes that, at the recommended dose of 0.5 mg/lb of body weight administered every 3 weeks, over-aggressiveness (in horses) is a potential adverse reaction to Equipoise. This aggressiveness may persist for 6–8 weeks after drug administration.

As cited in the case report of Dr. Dalby, this man was self-administering Equipoise on a 5-week escalating dosage schedule, ($\frac{1}{2}$ cc per day, 4 days a week, with increments of $\frac{1}{2}$ cc per week). Assuming that he used the 50 mg/ml formulation, he received 100 mg of Equipoise the first week of the cycle, 200 mg the second week, 300 mg on the third week, 400 mg on the fourth week, and 500 mg on the fifth week. Consequently, this individual took a total incremental dose of 1500 mg of a long-acting anabolic steroid, which for a 150 lb man, would be an amount that is 20 times higher than that which may produce long-term aggression.

Dr. Dalby's assertion that anabolic steroids have the potential for inducing behavioral effects when administered "even in limited quantities" seems misconstrued given the significant amount of steroid self-administered by the subject in this case report. The fact that the drug effects persisted beyond the immediate period of self-administration may plausibly be explained by significant drug accumulation due to the subject's rapid incremental multiple dosing schedule and the long half-life of the depot steroid preparation (2).

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HOWARD B. MOSS, M.D.
GEORGE L. PANZAK, R.N., M.S.
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Dr. Dalby Replies

SIR: Several clinical reports have demonstrated the adverse behavioral effects of anabolic androgenic steroids in athletes

and body builders. Uzych (1) noted that steroids are typically used by these individuals over an extended time period (8–240 weeks) and at dosage levels 10–100 times greater than therapeutic levels. Most steroid users combine or "stack" several steroids concurrently. I reported a case of a young man who showed sustained, radical behavioral change after his use of a single steroid of a dose low by human-use standards (2) for only 5 weeks. No previous report had shown a steroid-correlated transformation with such casual use. Dr. Moss and Mr. Panzak question whether my case can be considered as an example of brief exposure or low dose. The steroid used (Equipoise) is an equine preparation, and Dr. Moss and Mr. Panzak employ the manufacturer's suggested dose for horses and convert it to a human equivalent. The result, they conclude, is that the patient I reported had received a relatively high dose (compared to horses) and for a longer period than suggested by the manufacturer. Interspecies comparisons of drug response are rarely simple due to the many metabolic differences that exist. It seems clear that human users have paid little attention to the manufacturer's suggestions about use in establishing preferred dose. Dr. Moss and Mr. Panzak assist us by pointing out that what human users of steroids have established as "low" doses may be anything but. The behavioral response I reported is likely very common (in humans as in horses) and, as my case noted, the behavioral response of both humans and horses could persist beyond the period of drug use. The argument against any innocent use of these substances is thus strengthened.

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J. THOMAS DALBY, PH.D.
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Organic Mental Disorders

SIR: Robert L. Spitzer, M.D., and associates (1) proposed to retire the term "organic mental disorders," which, according to them, "implies an outmoded mind-body dualism." Ironically, their proposal is confounded by the same mind-body dualism that they wish to overcome.

For example, in Alzheimer's disease, the authors would have us believe that dementia is a "secondary disorder," i.e., that the disease "causes" the dementia as its "effect." Therefore, patients with Alzheimer's disease would continue to be coded twice, once for Alzheimer's disease and again for dementia. In fact, there is only one disease and an unresolved semantic muddle.

Furthermore, if the mental aspects of Alzheimer's are secondary to the physical lesions, so are physical aspects, such as shouting, myoclonus, and gait disturbances. The physical and mental manifestations of Alzheimer's are merely two sides of the same illness. Such usage of "secondary" only expresses a truism—that clinical features of diseases are "secondary" to pathological findings. Additionally, the brain lesions of Alzheimer's are secondary to the etiology agent(s), but this is also a truism.

The conceptual muddle of the "organic mental disorders" remains because the problem is not where these authors at-

tempt to locate it. They have not noticed that *DSM-III-R* and the *ICD-9 Classification of Mental Disorders (ICD-9)* are both manuals of "disorders," a situation which is almost unique in medical practice. There are nine categories of "disease" in *ICD-9* (such as diseases of the circulatory system), and only two categories of "disorders" (endocrine, nutritional, and metabolic disorders, and mental disorders). Physicians generally diagnose "disorders" when there are functional rather than structural problems (e.g., an epigastric "disorder" as compared to ulcers). Except for psychiatrists, medical colleagues never refer to Alzheimer's disease as a "disorder."

Unlike "disorder," the term "disease" refers to a pathological process in a patient that has an etiology, specific symptoms, and host-resistance factors. This works for Alzheimer's disease and for other "organic mental disorders" but not for histrionic personality disorder or hypochondriasis. And while the day may come when the term "disease" will apply to schizophrenia, it does not do so at present.

Regarding the "organic disorders," Karl Jaspers' (2) decades-old proposal for three groups (axes?) of psychiatric illnesses is worth reviewing:

1. Known diseases with psychic disturbances. This category includes cerebral illnesses such as Alzheimer's disease; systematic diseases such as uremia; and "poisons" such as alcohol intoxication and carbon monoxide.

2. Schizophrenia and manic-depressive illness. While these do not yet qualify as diseases, the notion of a disease can function as a "guiding idea" through which they can be studied and treated.

3. Everything else. The notion of a disease can still guide investigations, although there are no clear-cut boundaries between these psychiatric problems and other nonpsychiatric problems and we are far from appreciating etiology, pathophysiology, or host-resistance factors.

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OSBORNE P. WIGGINS, PH.D.
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SIR: I read with interest the Commentary by Dr. Spitzer and colleagues regarding the proposed classification of organic mental disorders in the *DSM-IV* because of its relevance to the field of developmental disabilities. Individuals with severe or profound disabilities may present, for example, with drug-responsive aggressive or self-injurious behavior. These behavioral disturbances can be manifestations of primary neuropsychiatric syndromes in which irritability, overactivity, and other disruptions in CNS function are the primary features (1-3). The need to establish an appropriate diagnostic category for these disorders is an important clinical issue because there are, in many states, medicolegal mandates requiring that developmentally disabled individuals be given a psychiatric diagnosis before any drug treatment is initiated. In the *DSM-III-R* these individuals could be given a diagnosis of organic mental syndrome.

Although I agree in principle with the proposal by Dr. Spitzer and associates to differentiate between primary and secondary disorders, it is not clear to me how they propose to categorize the neuropsychiatric syndromes I have described. The proposed *DSM-IV* category, "secondary personality change due to a nonpsychiatric medical condition (4)," is one possibility, but I would argue that it is inappropriate to classify disorders whose first manifestations may begin during infancy and persist throughout life as secondary. Subsuming them under the category of mental retardation would also be inappropriate because they are not intrinsic behavioral disturbances associated with developmental disabilities. I would suggest that the *DSM-IV* provide a distinct category, independent of the primary versus secondary dichotomy, for these disorders.

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SIR: The arguments of Dr. Spitzer and colleagues favoring deletion of the term "organic mental disorders" in *DSM-IV* suggest that these colleagues, like many wise philosophers both ancient and modern, remain troubled by the dilemma of the mind-body relationship (1). Despite their inference that Cartesian mind-body duality belongs to the past and that organic-nonorganic distinction is irrelevant because "of the growing body of evidence of the importance of biological factors in the etiology of major 'nonorganic' mental disorders," psychiatry cannot maintain its credibility unless there is differentiation between mental illness produced by verifiable biological causes and mental disorders related to the human condition and understandable in terms of psychological reactions to intrapsychic conflict, disturbed interpersonal relationships, or other adverse environmental factors.

The use of organic terminology implies the assumption of medical responsibility as the means for primarily alleviating or curing the illness. Nonorganic terminology implies patient responsibility toward restoration of normal mental function assisted by psychosocial support systems and, if necessary, symptomatic relief by the use of psychotropic medications. Eliminating the organic-nonorganic dichotomy will fuel skepticism that myriads of variant human behaviors are being medicated by psychiatrists simply because of presumed biology and thus absolving patients from self-responsibility for psychological rather than biologically proven mental disorders.

Despite its extensive use and popularity, *DSM-III* and its progeny have not escaped criticism (2, 3). Adding to *DSM-III*'s emphasis upon empirical description and ignoring causation by eliminating organic-nonorganic dichotomy (essentially the mind-body conflict) produces a woolly categorization of disorder.

ders that the authors mentioned (schizophrenia, hypothyroidic depression, and substance-related brain disorders) into their new classification of "primary," "secondary to a nonpsychiatric disorder," and "substance-induced disorder." No matter how useful such a ploy might be in preventing disharmony between the different schools of psychiatry, it represents an escape route when questions about whether functional major mental disorders are really biological arise. At least the term "nonorganic" differentiated from "organic" undeniably implies that psychiatry is not certain of an underlying organic basis for major functional mental disorders such as schizophrenia, this despite findings of associated brain abnormalities by no means proving causality (4, 5). I fear that under the cloak of "organic mental disorders" it is really the term "nonorganic mental disorders," with the obvious problem that the biological nature of these conditions is far from proven, that Dr. Spitzer and his coauthors wish to retire.

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THEODORE PEARLMAN, M.D.
Houston, Tex.

SIR: Dr. Spitzer and colleagues proposed eliminating the term "organic" and reorganizing the classification of organic mental disorders in *DSM-IV*. While I am in sympathy with their proposal in general, some aspects of it deserve closer examination.

First, the authors define secondary disorders as "due to medical disorders that are classified outside the mental disorders section of *ICD* (e.g., brain tumor, vascular disease, metabolic disturbance)." Their use of "secondary" here implies that the physical condition (nonpsychiatric medical disorder) should have an etiologic relationship (possibly pathophysiologic) with the secondary mental disorder. However, while acknowledging that it is often difficult to make a judgment about the etiologic role of physical conditions in mental disorders, Dr. Spitzer and colleagues do not provide any guidelines with which to test whether a physical condition has an etiologic relationship with a mental disorder. This lack of specific guidance has also been a limitation of *DSM-III* and probably reflects the incomplete nature of our understanding of this area.

Second, the relationship between a physical condition and a mental disorder often becomes more complex the more it is studied. For example, in the study of mood disorder following stroke, while early reports suggested a specific association between brain lesion characteristics and depression, further work has not always reproduced the lesion findings and has highlighted the role of other potential etiologic factors. These risk factors include family history of affective disorder, past psychiatric history, premorbid personality neuroticism traits,

negative life events (beyond the stroke itself), inadequate social support, and severity of disability, particularly among males. The findings indicate that the effects of stroke (such as threat to life, loss of function, role disruption) other than direct brain injury are also important in vulnerable individuals. Thus, given the complexities outlined above and the current lack of clear guidelines to determine the etiologic role of a physical condition, I suspect that the term "secondary" will often have little meaning other than a temporal relationship.

Third, in part, Dr. Spitzer and colleagues justify their introduction of secondary disorder by suggesting it will direct the clinician to the detection and treatment of underlying physical disease. While their intent is laudable, I wonder whether we need to design a classification system to address this issue of differential diagnosis. Perhaps undergraduate, residency, and continuing medical education would be a more appropriate vehicle?

Fourth, by limiting the category of secondary disorders to those with a relationship to physical conditions, Dr. Spitzer and colleagues introduce an etiologic component to *DSM-IV*. This seems to be a move away from the descriptive nature of *DSM-III* and *DSM-III-R*. However, to be consistent, other potential etiologic factors should also be given due recognition in the new classification.

Finally, like Fogel (1), my inclination would be to maintain a descriptive axis I nosology. If an etiologic subclassification for each mental disorder is required, then a list of possible etiologic factors (physical, psychological, and social) based on the available empiric evidence could be provided. Depending on the case at hand, the clinician would note the applicable factor(s), recognizing that in many cases the etiology would be unknown.

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PHILIP L.P. MORRIS M.D., Ph.D.
Baltimore, Md.

SIR: The proposal by Dr. Spitzer and associates to drop the term "organic mental disorder" from the *DSM* is well stated and deserving of further study and favorable consideration.

However, careful thought also should be given to possible opportunistic misinterpretation of these well-intended refinements by third party payers seeking simplistic and self-serving words to justify perpetuation of discriminatory health care coverage of mental illness.

The precise meaning and intent of these conceptual and linguistic changes should be clearly defined in any future diagnostic manual to minimize and counteract predictable legal arguments challenging favorable court decisions based on a physical-medical model of many major mental illnesses.

THOMAS T. TOURLENTES, M.D.
Galesburg, Ill.

SIR: Finally! Dr. Spitzer and colleagues' advocacy for eliminating the term "organic mental disorders" in *DSM-IV* is a long-overdue expression of common sense combating anachronistic obfuscation. There is no rational reason that schizophrenia and bipolar disorder should be labeled "functional" as opposed to "organic": at best this misleadingly suggests

causal explanations running counter to current consensus understanding; at worst it interferes with treatment and promotes inappropriate guilt in patients and their families.

One implication of this elimination not mentioned by Dr. Spitzer and colleagues, salutary in my opinion, would be the effect on admission criteria for various health facilities, e.g., state hospitals. Beleaguered though many of these institutions may be, their now-popular adoption of the adjective "organic" in front of any principal psychiatric diagnosis serving as an exclusionary criterion for admission, has been a cynical solution. This has encouraged misplaced attitudes of entitlement in accepting institutions' staff and promoted frustration and manipulation of diagnoses on the part of sending institutions' staff (often also beleaguered). We truly have enough difficulties with cynicism arising from external challenges without having to generate more for ourselves. Eliminating the "organic" terminology will at least repair an artificial division: the patient chronically psychotic following head trauma, surgery or stroke, etc., should not be arbitrarily excluded from the same range of dispositions as that of someone with schizophrenia. Rather, transfers and placements should be based on individualized, reasoned clinical judgments and criteria.

I'm less enthusiastic about the proposed use of "primary" and "secondary": why should mania following a stroke be considered "secondary" and mania proceeding from its undiscovered cause or causes be called "primary"? Admittedly, however, a better alternative has not occurred to me.

Emboldened by Dr. Spitzer and colleagues' laudable and ambitious proposed terminological reform, would it be too much to hope that we might consider an alternative to the term "schizophrenia"? "Split mind" is hardly an accurate or neutral image, and this etymological derivation has hopelessly popularized confusion with "multiple personalities" in common parlance and "humor" in the media. This has only added to shame and stigma for patients and their families. We could resurrect the variously used but more appropriate "paraphrenia," or find a new coinage.

WILLIAM M. GREENBERG, M.D.
Paramus, N.J.

Dr. Spitzer and Associates Reply

SIR: We appreciate this opportunity to respond to the very thoughtful comments on our article.

Drs. Schwartz and Wiggins suggest that our proposal is confounded by the same mind-body dualism that we wish to overcome. A mind-body dualism, which we agree is outmoded, is not the same as the dualism that our proposal perpetuates: the practical distinction between disorders/diseases classified within the mental disorders section of ICD and those classified outside. The suggestion that, for example, a depressive syndrome that is attributed by the clinician to hypothyroidism should be called "secondary depressive disorder due to hypothyroidism" (rather than "organic depressive disorder" as in *DSM-III-R*), has practical utility: it directs the clinical attention to the underlying endocrine condition. We fail to see how this is a perpetuation of a mind-body dualism.

Of course, saying that Alzheimer's disorder (the *DSM-IV* mental disorder) is due to Alzheimer's disease (the neurologic disorder) conveys no useful information. What Drs. Schwartz and Wiggins overlook is that Alzheimer's disorder (disease) is unique in that, ever since *DSM-III-R*, both psychiatry and neurology have insisted that the condition be classified within

their section. The Solomonesque solution to this turf battle was to include the disorder in both sections with slightly different wording, leading to the semantic muddle for this disorder that Drs. Schwartz and Wiggins refer to. However, numerous other examples illustrate the utility of our proposal for other dementias, such as the dementia due to HIV infection, head trauma, or endocrine disturbance.

Finally, Drs. Schwartz and Wiggins are uncomfortable with *DSM's* lumping of true diseases (e.g., the "organic mental disorders") with possible diseases (e.g., schizophrenia) and with supposed nondiseases (e.g., histrionic personality disorder), all under the umbrella rubric of "disorders." They would have us reconsider Jaspers' proposal for three groups, but we fail to see how such a proposal is relevant to the issue of whether our terminology, "secondary disorders," is preferable to the *DSM-III-R* terminology of "organic mental disorders."

Dr. Sovner asks how, with our proposal, *DSM-IV* would classify individuals with severe developmental disabilities which are manifestations of "primary neuropsychiatric syndromes." If the clinician judges that the disabilities are due to a diagnosable neurologic or other condition classified outside of the mental disorders section (e.g., secondary to head trauma, cerebral palsy), the diagnosis would be either "secondary personality change" (if there is an identifiable change in personality functioning) or else, "secondary disorder, not otherwise specified." The tougher problem is when there are symptoms (such as "soft signs") that suggest a neurologic disturbance, but inadequate data to confirm the existence of a particular neurologic diagnosis. There is no adequate diagnosis for such cases, which in both *DSM-III-R* and *DSM-IV* would by default be termed, "mental disorder not otherwise specified."

Dr. Pearlman appears to wish to perpetuate the very dualism that our proposal is designed to overcome. He believes that our proposal will inhibit attempts to answer a question that he regards as meaningful: whether "functional mental disorders" are really biological." We believe such a question is no longer appropriate and would sharply disagree with his notion that only patients with nonbiological disturbances have some responsibility for restoration of normal functioning. Does not the patient with diabetes or coronary artery disease (biologic disorders) have some responsibility for lifestyle changes and medication compliance that involve responsibility?

Dr. Morris is correct in noting that our proposal does not help the clinician make the extremely difficult *DSM-III-R* judgment as to whether a coexisting nonpsychiatric medical disorder is etiologically related to a presenting behavioral disturbance. Hopefully, the *DSM-IV* text will provide some useful guidelines to what will always be a difficult clinical decision. We would argue, however, that as difficult as the distinction often is in clinical practice, it has important educational and treatment implications that need to be preserved, in some form, in our nosology. Perhaps it would be better to make the etiologic distinction a subtype of a purely descriptive classification, as Fogel has suggested, and include, as Dr. Morris suggests, other potential etiologic factors, such as psychological and social factors. However, our proposal had to maintain consistency with the overall classification of *ICD-10*. Furthermore, noting the presence of etiologic, psychologic, or social factors for disorders in all of the major diagnostic classes, as Dr. Morris suggests, is unlikely to have as clear prognostic and treatment relevance as noting the presence of an etiologic nonpsychiatric medical disorder, which is the essence of our proposal.

We share with Dr. Toulentès the concern that the *DSM-IV*

will be scrutinized by third party payers in order to justify perpetuation of discriminatory health care coverage of mental illness. We would hope that our proposal could be used to further underscore the basic principle that biological factors may be of importance in *all* mental disorders.

Dr. Greenberg notes that one salutatory effect of our proposal will be to foil attempts of some psychiatric facilities to inappropriately exclude psychiatric patients from care who have "organic" problems. Emboldened by our attempts at terminologic revision, he proposes doing away with the term "schizophrenia." Like many traditional terms (e.g., conversion disorder, multiple personality disorder), one has to balance the advantages of familiarity and historical tradition with the advantages of picking a term that is more technically precise. In the case of schizophrenia, its long historical tradition and, in our judgment, no suitable alternative term, would seem to us to justify its continued use. Finally, we are also not entirely satisfied with the term, "secondary," but like Dr. Greenberg, we have been unable to come up with a better alternative.

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New York, N.Y.

Dopamine in Schizophrenia

SIR: In their article on the role of dopamine in schizophrenia, Kenneth L. Davis, M.D., and associates (1) reviewed relevant neurochemical studies. I recently performed a similar review (2) and came to a somewhat different interpretation. Dr. Davis and associates interpreted the evidence to suggest that mesocortical dopamine pathways may be deficient in schizophrenia, while mesolimbic dopamine pathways are overactive. My interpretation was that overall dopamine output is both deficient and hypervariable with periods of effective hyperdopaminergic function during acute exacerbations. These periods of effective hyperdopaminergic function could result from relative increases in dopamine release impinging on supersensitive postsynaptic receptors. Reduced dopamine output could cause postsynaptic supersensitivity by chronic synaptic depletion of transmitters.

Several factors are not fully explored by Dr. Davis and associates. First, their interpretation is based on an assumption that elevated dopamine levels in post-mortem studies indicates hyperdopaminergia when in fact it more likely indicates the opposite. Pharmacologic studies in animals demonstrate that when dopamine turnover is varied, dopamine levels and dopamine metabolite levels have an *inverse* relationship implying a build-up of unreleased dopamine when turnover decreases (3). The interpretation that increased dopamine levels indicates hypodopaminergia is supported by a study which showed that cerebrospinal fluid levels of dopamine-sulfate and dopamine metabolites vary inversely relative to various symptoms in schizophrenic patients (4). Other essential concepts in interpreting these studies involve the dynamic nature and longitudinal course of schizophrenia. Most studies of dopamine metabolite levels have found no difference in the dopamine turnover of schizophrenic patients and controls. However, these studies were generally performed on schizophrenic patients admitted for acute psychosis. Dopamine turnover

correlates positively with acute positive symptoms and negatively with chronic negative symptoms and severe pathology. Longitudinally, dopamine turnover falls with recovery from acute exacerbations whether or not neuroleptics are utilized (5). Furthermore, dopamine turnover decreases with age in schizophrenic patients but increases with age in normal controls. Schizophrenic patients who are older or have more chronic negative symptoms tend to have fewer acute exacerbations. Most studies have therefore selected a biased sample of patients, who have relatively high dopamine turnover and tested them when their dopamine turnover was relatively increased. Studies of chronic treatment-refractory schizophrenic patients have consistently demonstrated reduced dopamine turnover. This all suggests that in the baseline state, all schizophrenic patients have some degree of reduced dopamine turnover. No study has found evidence of increased dopamine transmission in schizophrenia.

These two interpretations are not necessarily at odds. It is quite likely that a disorder resulting in deficient dopamine output would affect the various dopamine tracts differently due to different protein populations (receptors, second messengers, cotransmitters, etc.), neurocircuitry, and regulatory mechanisms. Furthermore, a dopamine deficiency could lead to brain areas with hyperactivity if dopamine is acting as an inhibitory transmitter for that area (6). As a principal foundation, however, I believe that the interpretation that dopamine output is deficient and hypervariable is more consistent with the clinical experience of schizophrenia, an illness of chronic symptoms with acute exacerbations, and with the reviewed studies.

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ANDREW J. HERITCH, M.D.
Milwaukee, Wis.

Dr. Davis Replies

SIR: Dr. Heritch states that in his review on the role of dopamine in schizophrenia he reached a "somewhat different conclusion" than we did in our review. Dr. Heritch hypothesizes that dopamine output is both deficient and hypervariable, with increased dopamine function during exacerbations. In fact, this conclusion shows important similarities with ours, except that we proposed specific anatomical areas of increased and decreased dopamine activity, as well as a unifying hypothesis linking the two conditions. Specifically, we proposed decreased prefrontal dopamine activity (clinically reflected as

negative, deficit symptoms) and increased mesolimbic dopamine activity (clinically reflected as positive symptoms) to co-occur. We have hypothesized that the two conditions may be linked, i.e., decreased prefrontal dopamine function may lead to disinhibition of subcortical dopamine activity. Recently another attempt has been made to link states of decreased and increased dopamine activity, which appears to elegantly complement our hypothesis. Grace (1) hypothesized that decreased tonic activity of (predominantly prefrontal) dopamine neurons (clinically reflected in negative symptoms) would lead to compensatory upregulation of the dopamine system (predominantly subcortically) which would make it more sensitive to increased phasic release of dopamine (clinically expressed as positive symptoms).

The statement by Dr. Heritch that the post-mortem studies suggest decreased dopamine function is based on studies examining dopamine, not its metabolite, homovanillic acid (HVA) in post-mortem brain. Most post-mortem studies found both dopamine and HVA to be increased, suggesting increased dopamine turnover. Whether this also implies increased dopamine function depends on the state of the various dopamine receptors. Although studies have so far been confined to dopamine 1 and dopamine 2 receptors, their results suggest that dopamine 2 receptor sensitivity is increased in schizophrenic brains.

In summary, we agree with Dr. Heritch that states of decreased and increased dopamine activity can co-occur. However, we feel that our hypothesis as well as that of Grace linking different states of dopamine function to specific anatomical areas linking the two conditions has heuristic value until it will be replaced by other, more sophisticated, models.

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KENNETH L. DAVIS, M.D.
New York, N.Y.

Amobarbital Interview for Catatonic Patients

SIR: W. Vaughn McCall, M.D., and associates (1) are to be commended for their study of the amobarbital interview for catatonic patients. Revisiting old procedures is a valuable contribution.

I do wish to raise a question about the design of their study. Do they really believe subjects could not distinguish a saline infusion from an infusion of sodium amytal? Or that the "blind" judges did not notice the slurred speech, facial musculature relaxation, sleepiness, nystagmus, etc., that occur with the active substance? I seriously doubt it. What they in fact have is an experimental procedure that compares the response to a heavily tranquilizing medication to a substance that produces no pharmacological effects.

Aside from the significant biochemical differences that such a design results in, there is the very simple effect of the *experience or sensation* of sedation on a psychotic individual. How did the patients interpret this sensation? I would propose a simple counter-hypothesis. Those patients who were responders felt compelled or assisted in speaking as a response to the powerful sensations that the amytal produces. My experience with catatonic patients is that they are very preoccupied with notions of control and the impact of their voluntary move-

ments on maintaining control. For example, a common catatonic delusion is the belief that movement of any kind will result in world destruction. Given this belief system I do not think it unreasonable to suppose that the experience of the physician or investigator effecting the "heaviness" of their limbs via sedation might have a significant impact on their behaviors.

The failure of the authors to include a psychological hypothesis is part of a larger issue regarding the scientific validity of double-blind studies. Should we begin to consider that a "valid" double-blind medication procedure must involve inquiring whether the judges and subjects can determine experimental from control medication and what their expectations regarding each are?

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MICHAEL SACKS, M.D.
New York, N.Y.

Dr. McCall Replies

SIR: Dr. Sacks is correct in assuming that most of the subjects in our report had nonspecific signs of sedation while receiving amobarbital such as muscular relaxation, sleepiness, and slurred speech. Remember, however, that all the subjects were mute upon entry into the study; hence any sustained speech production (slurred or unslurred) must be taken as evidence of a therapeutic effect which was not seen with the placebo injection. Second, it may be difficult to distinguish between catatonic unresponsiveness and true sleep; sleepiness per se, therefore, did not routinely undo the blind method. Furthermore, the finding of the superior effectiveness of amobarbital compared with placebo was confirmed by an independent rater of the videotaped interviews. The additional "distance" interposed between the subjects and the rater by the videotape helps to eliminate some of the subtle clinical nuances that can only be felt when a rater is actually in the interview room with the subject. I believe this "distance" helped to ensure the blindness of the videotape rater. Dr. Sacks also questions that the subjects' response to amobarbital was a specific pharmacologic response (e.g., GABA-ergic), but may be instead a result of the subjects' interpretation of the nonspecific sedative effects of the drug as an opportunity to stop catatonic behavior. We were careful to state in our paper that there is not sufficient evidence to support the involvement of a specific neurotransmitter system. On the other hand, the combination of placebo and suggestion was insufficient to relieve catatonic symptoms. We reasoned, therefore, that some change in the patient's physiology was necessary for the rapid relief of catatonic mutism, and that neither a patient's expectations nor a purely psychologic intervention alone was sufficient. Whether a change in a patient's physiology (e.g., with amobarbital) alone is sufficient to break catatonia, or whether a physiologic change must be coupled with a patient's fertile expectations is an interesting but unanswerable question.

W. VAUGHN MCCALL, M.D.
Winston-Salem, N.C.

Anne Sexton's Biography

SIR: In the book review by Donald W. Goodwin, M.D. (1), of *Anne Sexton: A Biography*, Dr. Goodwin discusses Sexton's therapy and many diagnoses and writes of her psychiatrist Martin Orne, M.D., whose audiotapes of 300 therapy hours with Sexton were given to her biographer without her written consent. I am familiar with the arguments that have appeared in the press and medical journals about his behavior in releasing not only the tapes but also his clinical notes. The reviewer makes this defense: "He had the family's consent. Self-revelation was Sexton's forte—no one (sic) doubts she would have approved. Orne didn't receive a penny in compensation. For a true confessor, perhaps the more to confess about the better. If so, nothing could have pleased Anne Sexton more than this most revealing of biographies."

To state that "no one doubts she would have approved" is a fantasy. I doubt it. So have others. When do children have the rights to their parent's psychiatric notes? Sexton's daughter's relationship with her mother was at best problematic. Sexton did not even know of the existence of the tapes in Orne's possession. If it is true that, as Dr. Goodwin says, "for a true con-

fessor, perhaps the more to confess the better," why don't we hear about her sexual liaison with her next psychiatrist, which she confesses she wanted to expose. Why did the reviewer fail to mention this affair of the so-called true confessor? Is not *this* story of importance to the readers of the *Journal*?

The psychiatric profession is repeatedly attacked by many people as lacking the ability to implement its honorable and well-known ethics of confidentiality and condemnation of sexual exploitation. As Dr. Goodwin says, "Orne didn't receive a penny" in compensation for release of records and tapes. But her other psychiatrist got his regular fees for his service. I find that this enthusiastic review does a disservice to psychiatry by closing one eye. You do not hide shame by sham.

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HARRY A. WILMER, M.D., PH.D.
Salado, Tex.

Reprints of letters to the Editor are not available.

Corrections

In the reply by Owen M. Wolkowitz, M.D., et al. to the letter "Antiglucocorticoid Effects of DHEA-S in Alzheimer's Disease" (August 1992, p. 1126), there are several changes involving references. In the 20th line of the second paragraph, reference "2" rather than "4" should follow the word "rats," and in the next line, references "5" and "6" should follow "activities." In the third paragraph, the first sentence should end with reference "7." On the ninth line of that paragraph reference "6" should follow the word "imbalances" and in the next line reference "7" should follow "pregnenolone." Reference 6 is "Roberts E, Fitten LJ: Serum steroid levels in two old men with Alzheimer's disease (AD) before, during and after oral administration of dehydroepiandrosterone (DHEA). Pregnenolone may become rate-limiting in aging, in *The Biological Role of Dehydroepiandrosterone (DHEA)*. Edited by Kalimi M, Regelson W. Berlin, de Gruyter, 1990, pp 43-63." Reference 7 is "Flood JF, Morley JE, Roberts E: Memory enhancing effects in male mice of pregnenolone and steroids metabolically derived from it. *Proc Natl Acad Sci USA* 1992; 89:1567-1571." Also, please note that Eugene Roberts, Ph.D., is from Duarte, Calif.

In the letter "Addition of Fluoxetine to Clozapine" by Shawn L. Cassady, M.D., and Gunvant K. Thaker, M.D. (September 1992, p. 1274), the phrasing in the fifth line of the first paragraph should read "concomitant use of clozapine and fluoxetine."

The Listening Healer in the History of Psychological Healing

Stanley W. Jackson, M.D.

***Objective:** The purpose of this paper is the assessment of the healer's listening as an aspect of the history of caring and curing, with particular attention to its place in psychological healing. **Method:** An extensive range of philosophical, religious, and medical sources from antiquity to the present were studied. **Results:** Over the centuries, listening has been a crucial aspect of the various endeavors undertaken by healers in the interest of acquiring information from, achieving understanding of, and bringing about healing effects for sufferers. Yet it has been vision rather than hearing that has been emphasized in knowing and understanding, and looking rather than listening that has been emphasized in healing endeavors. Only around the turn of the twentieth century did there emerge the focused study of care in listening, of listening beyond the words themselves, and of the significance of the interested listener as a soothing, empathic force. **Conclusions:** The place of listening in depth and with empathy is a crucial element in healing. While the emphasis on looking remains significant in the gathering and appraisal of data, at times it threatens to overwhelm the need for an attentive and concerned listener. There appears to be a natural tension between the two modes that has, in modern times, been translated into a tension between a scientific mode of gaining information and a humanistic mode of knowing sufferers. A healer neglects either one at his or her peril—and at the peril of his or her patients.*

(Am J Psychiatry 1992; 149:1623–1632)

I should first note that the term “psychological healing” is used to denote a broad range of mental, psychic, or psychological interventions that have served healing, or at least ameliorative, purposes over the centuries. The array of twentieth-century psychotherapeutic interventions would be subsumed as species within this genus, along with many other psychological interventions, new and old.

Among other things, a healer is commonly a person

to whom a sufferer tells things; and, out of his or her listening, the healer develops the basis for therapeutic interventions. The psychological healer, in particular, is one who listens in order to learn and to understand; and, from the fruits of this listening, he or she develops the basis for reassuring, advising, consoling, comforting, interpreting, explaining, or otherwise intervening.

One author—an authority on communication—has said: “To be human is to speak. To be abundantly human is to speak freely and fully. The converse of this is a profound truth, also: that the good listener is the best physician for those who are ill in thought and feeling” (1).

Another authority—a psychological healer *par excellence*, the late Frieda Fromm-Reichmann—termed listening “a basic psychotherapeutic instrumentality.” She said that, if she were asked to state in one sentence what were “the basic requirements as to the personality

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and the professional abilities of a psychiatrist," she would reply, "the psychotherapist must be able to listen." For her, this meant "to be able to listen and to gather information from another person in this other person's own right, without reacting along the lines of one's own problems or experiences" (2).

SEEING AND HEARING IN KNOWING AND UNDERSTANDING

Visualism has held a primary position in the history of thought. Both the emphasis on direct visual referents and the predominant use of visual metaphors in the history of man's thinking about reality and experience were reflections of a primary emphasis on vision in studying natural phenomena and in developing explanations for how man knows things. This emphasis on vision was a central theme in classical Greek philosophical thought: In large measure, what these Greek thinkers knew was what they had seen. As the five senses were gradually differentiated from one another as sources of information, seeing was accorded the predominant position in the acquisition of knowledge. From "insight" to "enlightenment," and beyond, our language continues to be replete with visual metaphors in the language of knowing (3). Associated with this emphasis on vision was a relative inattention to hearing, and this was even more the case with the other external senses. As Aristotle (384–322 B.C.) stated it in his *Metaphysics* (4),

All men by nature desire to know. An indication of this is the delight we take in our senses . . . above all others the sense of sight . . . The reason is that this, most of all the senses, makes us know and brings to light many differences between things.

In his *Sense and Sensibilia*, he referred to "smelling, hearing, seeing" as senses that, to those animals that possess them, "are a means of preservation . . . But in animals which have also intelligence they serve for the attainment of a higher perfection." He then gave special attention to seeing and hearing. As he had in his *Metaphysics*, he emphasized that "seeing . . . is in its own right the superior sense"; but he added, "for developing thought hearing incidentally takes the precedence." He went on to say that "it is hearing that contributes most to the growth of intelligence" (5); and, in *On the Soul*, he commented to the effect that hearing was necessary and crucial for the receiving of communication (6). Hearing continued to be accorded a special place as the sense that, by receiving speech, "mediated between minds"; and, through hearing, sound "as music" had "emotional quality" and could "be made a factor in the formation of the soul" (7). Still, though, seeing continued to be predominant in discussions of sensation and perception and to be emphasized in considerations of how knowledge was acquired. "In fact, throughout the Middle Ages, there was a tendency to ignore the other

senses and concentrate on vision, while expressing the conviction that the general principles applying to vision should also hold true for the other senses" (8).

THE LISTENING HEALER

In most of the recognized modes of psychological healing over the centuries, it is clear that the would-be healer, in some way or other, has taken some pains to learn about the sufferer's ailments or difficulties in the process of developing a basis for his or her healing efforts. Sometimes the sufferer has presented himself and his difficulties to the healer who has mainly listened and, in so doing, has acquired the data needed in order to plan a helpful endeavor. Often enough, the listening has been supplemented by questions to bring out further data. Sometimes data have been conveyed to the healer by family members or friends of the sufferer, whether by word of mouth or by correspondence. Again and again, talking has clearly been an important aspect of the sufferer's activity in informing the healer about his ailments and difficulties and in the ongoing interaction with the healer as a healing process has taken place. And so, complementarily, the healer's listening has been a crucial element as well.

These matters are obvious enough in examining historical materials about the distresses and ailments of sufferers and about the psychological healing endeavors undertaken in response to them, but it is almost totally by inference that this can be said. Very little is said about the listening aspect of these encounters and processes. It seems to have been quite taken for granted in the written accounts left to us.

Then the significance of listening can be inferred from another type of evidence, more obvious, albeit still somewhat indirect. This evidence comes from repeated indications to the effect that the troubled and the suffering have yearned for an interested and concerned listener. Particularly poignant instances of this yearning for a listener who cares are found in the Bible, in *The Book of Psalms*, where particular Psalms and their place over many centuries make it clear that listening has been viewed by many as having the potential to ease a person's distress and suffering: "Hear my prayer, O Lord, and let my cry come unto thee . . . incline thine ear unto me" (Psalm 102). "Lord, hear my voice: let thine ears be attentive to the voice of my supplications" (Psalm 130). "Lord, I cry unto thee: make haste unto me; give ear unto my voice, when I cry unto thee" (Psalm 141). "Attend unto my cry; for I am brought very low" (Psalm 142). Recognizing this need for someone to listen with nurturant attentiveness, Fleischman has aptly referred to "a God of listening" in discussing these yearnings. And he grouped such yearnings with "the need to be seen, known, responded to, confirmed, appreciated, cared for, mirrored, recognized, identified," as "the yearning for witnessed significance" (9). Further, this theme of the wished-for listener is an inherent aspect of the practice of prayer.

The significance of the listener is repeatedly present, albeit implicitly, in the long traditions of various psychological healing activities—such as consolation, persuasion, confession, or confiding—each of these being a long-established mode of ministering psychologically to distressed and troubled persons and of bringing healing relief. And, here and there, there are clear indications of distress in the face of a listener's inattention or unsatisfactory listening. For the most part, though, listening seems to have been taken for granted; and the predominant emphasis continued to be on seeing or looking as the means of obtaining information about and coming to understand suffering persons.

THE NINETEENTH CENTURY

The nineteenth century brought even further emphasis on seeing rather than hearing, on looking rather than listening, in the realms of sickness and healing. In the sufferer's appearance, in his visible behavior, there had always been thought to be evidence to aid the healer in understanding the sufferer's illness and to guide him toward appropriate treatment and accurate prognosis. Then, with the nineteenth century's accumulating populations of mentally ill persons who came under the observation of alienists and psychiatrists, a new tradition of seeing and looking developed which argued that significant correlations were there to be observed between the sufferer's appearance and his psychopathology. Physiognomy, or the study of human character through facial configuration, had long been considered a meaningful enterprise; and it had been specially furthered in the eighteenth century by the work of Johann Kaspar Lavater (1741–1801). Then, in the nineteenth century, Franz Joseph Gall (1758–1828) and Johann Kaspar Spurzheim (1776–1832) evolved the discipline of phrenology in which the bumps and contours of the head were thought to give evidence of mental faculties and character traits.

Against this background, Alexander Morison (1779–1866) presented his *Outlines of Lectures on Mental Diseases* in which he addressed the physiognomy of the insane and to which he added illustrative engravings; and, in 1838, he published *The Physiognomy of Mental Diseases* with over 100 plates of psychiatric patients aimed at demonstrating pictorially observable correlates of their mental illnesses. J.E.D. Esquirol (1772–1840) used illustrations of patients in his textbook, *Maladies Mentales*, in 1838. And, in the late nineteenth century, Jean-Martin Charcot (1825–1893) and Paul Richer (1849–1933) published extensively on correlations between appearances and psychopathological states. Within this context, in the 1850s, Hugh W. Diamond (1809–1886), a psychiatrist who succeeded Morison at the Surrey County Asylum, developed the work that was to earn him the title of “the father of psychiatric photography.” Among the uses he made of his photographs of the insane, a primary one was the photograph as a diagnostic tool with insane patients,

based on correlations of physiognomy and clinical states (10).

Out of these activities and their associated assumptions, there emerged a groundswell of support for the notion that looking at insane patients was the essential avenue to knowledge of their psychopathology. Attention to the shape of the face and the head, to the facial expression, to gestures and postures, and to body build was thought to be of central significance. The primacy of seeing in knowing had received new support.

It is well to be reminded that these trends in looking in order to know about the mentally ill evolved in an era in regard to which Michel Foucault (1926–1984) could refer to the new clinical medicine as essentially emerging out of an emphasis on seeing. In his *Birth of the Clinic*, he stated that “this book . . . is about the act of seeing, the gaze” (11). He went on to discuss “the clinical gaze” at some length and gave it a crucial place in the acquisition of clinical knowledge. By the end of the nineteenth century, the primacy of visual observation in medical knowledge in general was rarely questioned. It was against this background that listening gradually came to be attended to by healers in ways that it never had before.

“THE TALKING CURE” AND LISTENING

In the famous case of Anna O., the patient who was treated by Josef Breuer (1842–1925) in the early 1880s and whose treatment was so influential in the early development of the work of Sigmund Freud (1856–1939), the patient referred to the treatment as a “talking cure,” and Breuer used such phrases as “talked through,” “talked away,” and “talking out” to indicate the nature of the therapeutic activity (12). For all the emphasis on the patient's talking, though, it is consistently clear that the physician's role was also crucial and that his listening was a critical feature of that role. In reading about this clinical work, one takes the listening for granted, and it is clearly reasonable to do so. But it was only later, when thoughtful students of the Anna O. case were subjecting it to intensive study, that this theme of listening came to be made explicit. For example, Ellenberger aptly referred to “the tranquillising effect of Breuer's listening to the stories she told him” and observed that “he was able to soothe her by listening to her stories” (13, pp. 275–276). The emphasis on the therapeutic value of talking had always implied a meaningful listening as a complementary activity, but Ellenberger was identifying the further element of the soothing and healing effect of the listener's interested listening.

Years later, with his own development of psychoanalysis well advanced, Freud had something to say about listening. In his “Recommendations to Physicians Practising Psycho-Analysis,” he urged that the psychoanalyst not direct his “attention to anything in particular” and that he maintain “the same ‘evenly-suspended attention’ . . . in the face of all that one hears”

(14, pp. 111–112). In that essay he was advising against various determined efforts to remember and was urging an unbiased, open-minded listening to everything the patient had to say. He explicitly indicated that the psychoanalyst would thus remember more and with less intrusion of bias; and he implicitly indicated that such a way of listening would lead to the psychoanalyst hearing more. Freud said little else about the subject of listening, but this advice has influenced the manner of listening for many a clinician since that time. In fact, these recommendations of Freud's became central in considerations of listening in the teaching of psychoanalytic technique over many decades. (An effective and representative summary of how the analyst listens was provided by Ralph Greenson [15].) As Ricoeur was to state it later, "corresponding to the 'total communication' on the part of the patient is the 'total listening' on the part of the analyst" (16).

Theodor Reik (1888–1969) particularly emphasized this special approach to listening, though he preferred the term "free-floating attention" rather than "evenly-suspended attention." But Reik's considerations of the listening healer went much further, and he offered some profound observations on the subject in his book on "the inner experience of a psychoanalyst," *Listening with the Third Ear*. Borrowing the term "the third ear" from Nietzsche, Reik used this title phrase to refer to a capacity that he thought that a psychoanalyst needed to develop. The psychoanalyst needed "to learn how one mind speaks to another beyond words and in silence. He must learn to listen 'with the third ear.' " This "third ear . . . can catch what other people do not say, but only feel and think; and it can also be turned inward. It can hear voices from within the self that are otherwise not audible because they are drowned out by the noises of our conscious thought-processes." Reik was discussing the notion of the analyst sensing and resonating to feelings and listening for nuances and meanings that went beyond, or lay beneath, the spoken words. These references to listening meant a sensitive, discerning use of the sense of hearing, but he was also using listening to stand for all the senses. The analyst was urged to open "all his senses to these impressions" (17). In his silence the analyst was to provide a receptivity that was freeing to the patient and that thus facilitated a more profound communication from sufferer to healer.

EMPATHIC LISTENING

Empathic listening is a significant feature of modern thought on listening in healing contexts, but the term is a relative newcomer in the language of psychological healing. In order to appreciate how it has emerged, though, one has to consider the history of the parent term "empathy." The roots of the latter term are to be found in the thinking of Theodore Lipps (1851–1914) and his term *Einfühlung*. In 1872 Robert Vischer (1847–1933) addressed the question of an observer at-

tributing feeling and emotion to works of art and to forms of nature. He explained this in terms of some unconscious process in the observer endowing such objects with vital content. And he named it *Einfühlung*. Then, beginning in the 1890s, Lipps studied this extensively and effectively established the term *Einfühlung* for continued use. His original view belonged in the realm of esthetics and dealt with the attribution to or projection into an art object of a viewer's feelings (18). As Lipps defined it at one point, *Einfühlung* meant "feeling something, namely, oneself, into the esthetic object" (19, p. 302). Later, he came to include one person's appreciation of the feelings and attitudes of another person as one of the ways in which *Einfühlung* might be manifested (20, p. 184). The English term "empathy," with the meaning of "feeling into," became the accepted translation for *Einfühlung* after being suggested by Edward B. Titchener (1867–1927) in 1909 (21, p. 21).

There were various streams of development out of these origins, both in theory and in practice. But it was only slowly that the notion of empathy entered the clinical realm. Sigmund Freud was interested in Lipps's work and made several uses of the latter's concept of *Einfühlung* in his *Jokes and Their Relation to the Unconscious* in 1905. Although these were not clinical applications of the concept, some of them did entail "putting oneself into" the psychical state of another person, the one producing the witticism (22). Then, although it entailed empathy with a fictional person, a similar projection of oneself into the psychical state of another was mentioned in *Delusions and Dreams in Jensen's Gradiva* in 1907 (23). Perhaps more interesting to the clinician was Freud's use of the concept in his *Group Psychology and the Analysis of the Ego* in 1921. He referred to "the process which psychology calls 'empathy (*Einfühlung*)' and which plays the largest part in our understanding of what is inherently foreign to our ego in other people"; and he invoked it to explain group members' appreciation or understanding of one another. In his brief discussion he associated empathy with identification and with imitation, stating, "a path leads from identification by way of imitation to empathy, that is, to the comprehension of the means by which we are enabled to take up any attitude at all towards another mental life" (24). (Basch [25, p. 103] has urged a significant correction to this translation. Rather than empathy enabling us "to take up any attitude at all towards another mental life," he points out that the implication was that "empathy was indispensable when it came to taking a position regarding another person's mental life".) Although not a clinical application of the concept, it was a use that seems to have had implications for clinical contexts.

The first study in the psychoanalytic literature to address empathy explicitly as a factor in the clinical process seems to have been "The Psycho-Analytic Method of Observation" by Theodore Schroeder (1864–1953) in 1925. Focusing on "*empathic insight; empathic understanding; retrospective and inductive introspec-*

tion," Schroeder wrote, "the psycho-analytic method makes experimental use of empathy as a means of reading something out of the psyche of another." For the psychoanalyst or "empathist," this "empathic viewing of another's psyche involves a maximum of attention upon the associated affective tones, values and processes." He went on to say that "empathic insight implies a seeing (re-living) as if from within the person who is being observed. It is as if, by a conscious withdrawal of interest and by the exclusion from consciousness of all present relationship to everything else, one places one's own consciousness at the disposal of the unconscious determinants of another's personality" (26, pp. 159, 162). Surprisingly, from Deutsch and Ferenczi to Kohut and since, the psychoanalysts who have written about empathy have said nothing about Schroeder's paper.

In 1926, Helene Deutsch (1884–1982) briefly discussed "intuitive empathy" in clarifying the nature of seemingly occult events in psychoanalysis; and she did so in a way that took it for granted that it was not an unusual phenomenon in the psychoanalytic process (27, pp. 136–137). It is Sandor Ferenczi (1873–1933), though, who is usually thought to have been the first psychoanalyst to suggest explicitly that empathy is, and should be, an element in clinical work. In 1928, in "The Elasticity of Psycho-Analytic Technique," he introduced the notion of *tact* as a crucial factor in determining when the analyst should undertake an intervention, particularly an interpretation. He then raised the question, "But what is 'tact'?" and he answered, "It is the capacity for empathy." He then elaborated to the effect that, through empathy, having "succeeded in forming a picture of possible or probable associations of the patient's of which he is still completely unaware, we, not having the patient's resistances to contend with, are able to conjecture, not only his withheld thoughts, but trends of his of which he is unconscious." He went on to say that "this empathy will protect us from unnecessarily stimulating the patient's resistance, or doing so at the wrong moment." Further, the analyst's empathy served to protect the patient from unnecessary pain. He used the term "the empathy rule" for shorthand reference to these matters. He noted that the analyst's mind "swings continuously between empathy, self-observation, and making judgments." And he concluded by saying, "My principle aim in writing this paper was precisely to rob 'tact' of its mystical character" (28).

After Ferenczi, empathy was only rarely mentioned in the psychoanalytic literature over the next 25 years (29, 30). Then, in the 1950s, significant references to it began to increase (31–36). The situation prior to this is stated well by Roy Schafer, a significant contributor to the 1950s attention to empathy. "Comparatively little investigation and conceptualization of empathy can be found in the psychoanalytic literature; despite persistent emphasis on its importance in the therapeutic process, not to speak of child development and personal relationships" (35). Particularly influential among the 1950s contributors was Heinz Kohut (1913–1981),

whose work was to lead to the self psychology of today and whose emphasis on the role of empathy influenced psychoanalysis and psychotherapy in ways that brought empathy into the center of their clinical considerations (34). Then there was the work of Ralph R. Greenson (1911–1979), another member of this 1950s group, who wrote on "Empathy and Its Vicissitudes."

Most experienced psycho-analysts will agree that in order to carry out effective psychotherapy a knowledge of psycho-analytic theory and the intellectual understanding of a patient is not sufficient. In order to help, one has to know a patient differently—emotionally. One cannot truly grasp subtle and complicated feelings of people except by this 'emotional knowing.' It is 'emotional knowing,' the experiencing of another's feelings, that is meant by the term empathy. It is a very special mode of perceiving. Particularly for therapy, the capacity for empathy is an essential prerequisite. Although I believe these points are well known it is striking how little psycho-analytic literature exists on the subject of empathy . . . There seems to be a tendency among analysts either to take empathy for granted or to underestimate it (36).

It must be much more than a coincidence that Schafer, Kohut, and Greenson, apparently working quite independently of one another, came out with such vigorous espousals of the importance of empathy within a very short span of time. Individually and collectively, they have had a significant influence on psychoanalysis and psychotherapy in the 30 years since then; and empathy has become a common topic in the literatures of those disciplines.

Although often unacknowledged in the psychoanalytic and psychotherapeutic literatures, there were other scholarly traditions in which respectful attention was being paid to notions akin to empathy as ways of appreciating and knowing about the inner life of another person. As early as the beginning of the 1920s, social psychologists and sociologists were developing such ideas and studying their place in interhuman relationships. I would mention particularly Charles H. Cooley (1864–1929) and his "sympathetic introspection" (37) and George H. Mead (1863–1931) and his "role-taking" (38).

Turning again to clinical contexts, by 1951, when his *Client-Centered Therapy* was published, Carl R. Rogers' psychotherapeutic approach had come to have empathy as a recognized central element in its operations.

It is the counselor's function to assume, in so far as he is able, the internal frame of reference of the client, to perceive the world as the client sees it, to perceive the client as he is seen by himself, to lay aside all perceptions from the external frame of reference while doing so, and to communicate something of this empathic understanding to the client (39).

During the 1940s, Rogers had gradually developed this viewpoint, and it became the essence of what, in his clinical work, he meant by "client-centeredness."

These various notions of empathy vary somewhat in their details and in how they are used. But, whatever is

the case in a particular viewpoint, they all entail a coming to know about another through an imaginative experience of being in the world of his or her thoughts, feelings, and attitudes. One way or another, what is involved is a profound listening. The healer truly *hearkens* to the sufferer—that is to say, the effort is to hear *and* to know or understand.

While it has always been clear in the psychoanalytic literature that empathy entailed attentive listening to the patient, it was only after the increased, more focused attention to empathy in the 1950s that explicit references to listening became more frequent and even consistent. Greenson emphasized listening as a matter of course, but then made the point that “listening from the ‘outside’ ” was insufficient and that it had been crucial that he “shifted—from listening and observing from the outside to listening and feeling from the inside,” i.e., from an empathically attuned position (36).

Gradually, out of the self psychologists’ attention to empathy and the unavoidable, although often unstated, significance of the analyst’s listening, there emerged an increasingly explicit emphasis on psychoanalytic listening and on empathic listening in psychoanalysis and psychotherapy. Although clearly indebted to and influenced by Kohut in her attention to empathy and in her mode of practice, Evelynne Schwaber seems to have been crucial in bringing about these newer terminological practices. In a series of papers from 1979 to 1983, she discussed empathy as “a mode of analytic listening” and as “the listening perspective,” in relation to self psychology (40–42). She wrote about being used “as part of the core of the patient’s self” by a pathologically narcissistic patient and then went on to say

I slowly came to recognize that listening in this way—having to place myself inside the patient’s self experience—called somehow for another mode of listening, of perceiving, than one in which I would be positioned somewhat ‘outside’—that is, as target rather than subject of the patient’s affects, drives, and defenses (41).

Adding that “it is this listening stance which is what I mean by empathy,” she referred to empathy as “a specific, scientific mode of perceiving—the matrix of depth-psychological observation.” This “quality of listening,” this “subjective listening mode,” was “the empathic mode,” a “mode of psychological data gathering” (41). Schwaber argued that “each theoretical system may suggest a definition of the listening stance within its own framework,” but that, as a method of gathering data, empathy has a certain independence of theories. This listening mode or “listening stance attempts to minimize the introduction of an ‘outsider’ view.” She termed this listening stance “empathic listening” (40). Parenthetically, it should be noted that listening is certainly at the heart of the matter in *empathic listening*, and yet the use of the term “listening” in such contexts is partly an effort to capture metaphorically a very complicated process.

Already well attuned to the significance of listening

in psychotherapy, more recently Chessick has taken up the theme of empathic listening in a thoughtful and useful way. In his textbook of psychotherapy in 1974, he said that “it is clear . . . that listening, in a therapeutic sense, is an extremely active process. It occurs silently within the therapist and permits him fully to observe the patient’s behavior, as well as his own association and emotional responses to the material presented by the patient” (43). Then, in his recent book on listening in psychotherapy, listening is the central, organizing theme in a study of five different “listening stances” that might be assumed by a psychotherapist; and he addresses empathic listening in some detail. Noting that Schwaber’s approach introduces “an alternative mode of psychoanalytic listening from that of Freud,” he categorizes her “point of view as belonging to only one of the five models of theoretical understanding that must be used in a comprehensive listening process” (44).

DISCUSSION

Toward Listening

In the realm of psychological healing, the twentieth century has seen an increasing recognition of the significance of the healer’s listening in the healing process. And there are many indications of such a trend other than those just cited from psychoanalytic and psychodynamic therapeutic traditions. Turning to the context of a general physician’s consultation room, attentive, interested listening can turn an inchoate litany of complaints into a gradually coherent story of distress and discomfort. The patient is the better for having told the doctor, whether it has been a confessing, a confiding, a catharsis, or a revealing of physical symptoms that would have otherwise gone undetected; and the doctor is the better for having been *with* the patient in a healing endeavor rather than having rapidly gotten rid of him with the aid of a prescription pad. Often enough, the physician’s listening has allowed the emergence of more private concerns and symptoms that have been the issues that were more crucially in need of therapeutic attention.

Or, I can turn to an example from a medical student’s experience. This is a painful example of how a clinician struggled through a patient’s off-putting distress to listen in a deeply meaningful, and useful, way. I quote from Kleinman’s *Illness Narratives*.

The . . . patient was a pathetic seven-year-old girl who had been badly burned over most of her body. She had to undergo a daily ordeal of a whirlpool bath during which the burnt flesh was tweezed away from her raw, open wounds. This experience was horribly painful to her. She screamed and moaned and begged the medical team, whose efforts she stubbornly fought off, not to hurt her anymore. My job as a neophyte clinical student was to hold her uninjured hand, as much to reassure and calm her as to enable the surgical resident to quickly pull away the dead, infected tissue in the pool of swirling water, which rapidly turned

pinkish, then bloody red . . . I tried to distract this little patient from her traumatic daily confrontation with terrible pain. I tried talking to her about her home, her family, her school—almost anything that might draw her vigilant attention away from her suffering. I could barely tolerate the daily horror . . . Then one day, I made contact . . . uncertain what to do besides clutching the small hand, and in despair over her unrelenting anguish, I found myself asking her to tell me how she tolerated it, what the feeling was like of being so badly burned and having to experience the awful surgical ritual, day after day after day. She stopped, quite surprised, and looked at me from a face so disfigured it was difficult to read the expression; then in terms direct and simple, she told me. While she spoke, she grasped my hand harder and neither screamed nor fought off the surgeon or the nurse. Each day from then on, her trust established, she tried to give me a feeling of what she was experiencing. By the time my training took me off this rehabilitation unit, the little burned patient seemed noticeably better able to tolerate the debridement (45).

I would now like to consider briefly some of the generic ingredients that go to make up these various instances of invaluable listening. The effective healer in the realm of psychological healing tends to be someone who is interested in talking with and listening to the other person. And these inclinations are grounded in an interest in other people and a curiosity about them. Further, such healers have a capacity for caring about and being concerned about others, particularly about those who are ill, troubled, or distressed. The sufferer—ill, troubled, or distressed—tends to be someone who seeks out a healer who will be interested, concerned, and responsive to his distress, who will minister to his ailments, and who will bring him relief, if not cure. He seeks to be listened to, to be taken seriously, and to be understood, as crucial aspects of this process.

All this, in turn, is set in a context of human need for connection with other persons, for the intimacy of a relationship with another person, for relationships as antidotes to aloneness or being isolated, for the closeness or meaningfulness associated with such connections (quite distinct from a sexual relationship or an erotic attachment). And these needs for such relationships influence both sufferers and healers. For the sufferer there is a yearning to be listened to, to be valued, and to be understood. And the healer has his own need to listen, to understand, and so to bridge the divide between the two persons in the potentially healing dyadic relationship.

In situations such as these, the attentive listening of a concerned and interested healer can, and often does, have a compelling effect on the sufferer. The sufferer, often enough, responds by telling more about himself, by revealing more. The very process of the sufferer's confiding, in turn, commonly has a compelling effect on the listening healer. The listening and the talking, the talking and the listening, have a mutual attachment effect. The relationship is deepened—more is said, more is heard, more is understood, more of a sense of being understood is experienced. The term "the talking cure" is not without its relevance to such situations, but, at

best, the term is incomplete. The healer's listening is just as crucial; in fact, it is essential. While this listening must entail attentiveness and interest, the healer as listener is at the heart of the matter. The term "the listening cure" would be just as relevant. The sense that you have been listening, that you have tried to appreciate the sufferer's distress or dilemma, that you are concerned and have tried to understand, that your listening may have led to understanding, these things matter profoundly to a sufferer. They may help you toward a healing intervention, and they may help themselves even be healing in their effects. Perhaps we should say "the talking *and* listening cure."

Interferences With Listening

For all the increased recognition of the value of listening, there is, too often, an anxiety in the face of listening—perhaps I should say a fear of what might be heard and its disturbing, distressing effect on us as listeners. What we will hear, if we allow ourselves to listen, will be so disturbing, so terrible—be it about severe pain, about distress in the face of disabling disease, about panic, about the terror of inner disintegrative trends in a psychosis, or about horrible rememberings or relivings of past traumata. Or there might be some other communication that would stir disturbing feelings in a healer—anger, shame, guilt, sexual feelings. These moments in the sufferer-healer interaction can interfere mightily in listening to a sufferer, in learning about his difficulties, in coming to appreciate and understand those difficulties. These sorts of effects can block listening that could be essential to acquiring the understanding necessary to treat the sufferer reasonably well. They can preclude the use of the healer's empathic capacities that might be essential to learning about the sufferer's difficulties and providing the necessary healing interventions. They can influence healers to interrupt, to change the subject, to talk instead of listening, to keep away somehow from such troubling effects.

Useful, even essential, listening may be avoided by modern healers for other reasons, though. Sometimes explained in terms of the efficient use of a healer's time, sometimes determined by the intrusions of modern diagnostic technology, and sometimes accounted for by strivings to be scientific or at least objective, modern clinicians have often distanced themselves from patients, or have been distanced by a clinical structure, in ways that have seriously interfered with the valuable clinical listening that the twentieth century has come to appreciate. While anxiety or fear in the face of disturbing communications may be hidden within these other rationales, the latter do seem to be distinct interferences in their own right.

In a thoughtful history of doctor-patient relationships entitled *Bedside Manners*, Shorter takes some pains to demonstrate "the informal psychotherapeutic power of the consultation," which power he attributes to "the catharsis that the patient derives from telling his story to someone he trusts as a 'healer.'" Unfortu-

nately, as Shorter points out, the recent trend in medicine has been "to steer the consultation toward a single, identifiable physical problem, the 'chief complaint.'" Physicians have developed question-and-answer techniques in history-taking that move patients toward a chief complaint, a recognizable pattern of symptoms, and then to a basis for a prescription. Often enough, this process discovers a plausible excuse for the medical visit, while the real cause of the visit remains undiscovered. It seems that what has occurred is a shift from being patient-oriented to being disease-oriented. By reducing the opportunity for the patient to talk and avoiding the need for the doctor to listen, a type of efficiency has been achieved, but the cost has included the loss of healing opportunities, opportunities for psychological healing in the medical consultation itself. "The erosion of careful listening" has often meant the loss for patients of the "opportunity to say what is really troubling them" and of "the cathartic value of telling" their stories. Shorter points out that "listening is the main kind of informal psychotherapy the family doctor is able to conduct," that listening is a crucial ally for the doctor in helping his patients cope with psychological distress and mental disorders (46).

As previously suggested, there are still other ways in which the significance of listening is often lost sight of in contexts of sickness and healing. We are in an era of remarkable, almost incredible, advances in molecular biology in psychiatry—in medicine, in general. And various technological advances have allowed us to learn remarkable new things from patients that can guide our treatments. Yet these same technologies can also serve to distance us from patients. While seeing more, we are often at high risk of hearing less. From X-rays to modern imaging techniques, there is a comforting concreteness, a reassuring reliance on what can be seen. The readings derived from laboratory tests, too, so often provide a reassuring sense of visualizable certainty in the numbers on the page of a report. What the sufferer tells the healer is not viewed as being without significance, but, all too often, it quickly moves the healer toward a category of things to check out with his technologies and, sooner or later, to a category of concrete, material interventions: substances or procedures. The healer has listened in his special ways, but, all too often, has heard mainly through the filters provided by his categories of investigative procedures, his diagnoses, and his technologically based interventions. And somehow the sufferer has been put at a distance. The healer may listen more in narrowly categorized ways, and yet he will hear less and is in serious danger of attending less to the person. As Spiro has stated, "the physician looks for disease rather than listens to the patient. Yet illness, the patient's complaint, can only be understood by listening to what he says." Although the detection of disease may come from the image, "the diagnosis of illness comes from listening." "Listening is much harder work than seeing; it takes time, concentration, and active participation. But physicians need to listen as much as to look, to make all senses work together" (47).

CONCLUSIONS

There has been surprisingly little emphasis on the value and significance of clinical listening over the centuries. Even further, with the gradual emergence of modern clinical medicine in the nineteenth century, it was clinical looking, above all, that brought the most valued information for healers. The visual scrutiny of lesions and of the reflections of disordered function was considered significant above all other sources of data. The growing knowledge of pathological anatomy, both pre-mortem and post-mortem, supported this trend. The development of microscopy, associated staining techniques, and the fruits of the germ theory of disease all served to extend this trend. And, in keeping with what was happening in general medicine, it was thought that what the healer could see in the sufferer from mental illness was the royal road to knowing about that category of sickness as well.

Somehow, though, around the turn of the twentieth century, there was a reaction to all this, an emerging concern with listening to the sufferer. In psychoanalysis and other depth psychologies, what the sufferer could and would tell the healer, the need to facilitate such telling, the need to listen carefully, and the emerging emphasis on empathy as a listening stance were aspects of an increased sensitivity to the person of the sufferer rather than to the disease from which he suffered. Parallel developments in general medicine in the first several decades produced increased concerns about sufferers that were reflected in catch phrases such as "the doctor-patient relationship" and "the patient as a person"; and listening carefully to their patients was urged on physicians as it had never been before. As William Osler put it, "Listen to the patient; he is telling you the diagnosis" (attributed to William Osler, but exact source not identified).

The early twentieth century also saw imaging enter the medical field. With the X-ray, a special type of looking was born. Diagnostic efforts were greatly strengthened. And, at the same time as listening was being increasingly advocated, a more penetrating form of looking was influencing many physicians to rely less on listening. On the one hand, it became common to urge physicians to take time with patients, to allow patients to tell their stories, and to listen to them carefully. On the other hand, all too often physicians perceived themselves as being very busy and heavily burdened, and they took steps to streamline their practices and to save time. Questionnaire approaches to history-taking were introduced; and, sometimes, the taking of a case history was delegated to a nurse or other assistant. Increasing reliance on laboratory tests seemed to make listening even less significant. And the more recent advent of even more powerful imaging techniques took this trend even further.

The same century that has brought more concern with and attention to listening than ever before has introduced more interferences with and rationales for not attending to listening than ever before. Often enough,

patients complain that physicians are too busy, that they are not interested, or that they do not listen. As physicians strive to gather more data, to see more, to be more objective, to be more scientific, they are often experienced by their patients as not listening.

Around the beginning of the century, a growing tension was emerging between medical science and clinical medicine. Encouraged and emboldened by the scientific developments of the latter half of the nineteenth century, medical scientists were arguing for and acquiring a larger place in the medical world, including more respect, positions and departments in medical schools, and an increased influence on what was done therapeutically. As these important changes were occurring, a special dilemma was coming into focus to a degree that it never had before—to attend to the disease or to the sufferer? to treat the disease or to treat the patient? And our century has seen frequent oscillations between concerns about the science of the disease and the humanity of the patient.

Is it that there is, and always will be, a natural tension between looking and listening as ways of knowing? Or is it more a reflection of the tension between a scientific mode of gaining information and a humanistic mode of knowing the sufferers? Whichever it might be, there does now seem to be a well-established tension between attention to diseases and attention to suffering persons.

Speaking to the psychological healer, I would want to remind him or her that the healer who really listens will hear the dejection and sadness that is so often at the heart of anger, the anger so often enmeshed in dejection and despair, the fear so often at the root of hostility, the strength in weakness and the weakness in strength, the more deeply felt in the apparently more prominently felt. To physicians in general, I would ask, "How many of today's complaints about doctors stem from doctors not listening?" Listening is central to learning about and coming to understand a sufferer, and those steps are crucial to being a healer. The healer learns about the sufferer in direct proportion to the quantity and quality of his listening. And this is not to ignore looking, or to overlook disease, or to downgrade objectivity.

In closing, and with apologies to the author of *Ecclesiastes*, "To everything there is a season." A time to speak, and a time to hearken; a time to look, and a time to listen.

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Clinical and Research Implications of the Diagnosis of Dysphoric or Mixed Mania or Hypomania

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Objective: The authors reviewed available evidence regarding the status of dysphoric or mixed mania as a distinct clinical state and formulated operational criteria for its diagnosis. **Method:** Studies of dysphoric mania or hypomania in patients with bipolar disorder were analyzed with regard to clinical characteristics, prevalence, demographic features, course of illness, outcome, family history, associated conditions, biological tests, and response to biological treatment. **Results:** Although some studies suggest that dysphoric and nondysphoric mania are similar conditions, others suggest that, compared with nondysphoric mania, dysphoric mania may be more severe; more likely to occur in women; more likely to be associated with suicidality, a younger age at onset, a longer duration of illness, higher rates of personal and familial depression, concomitant alcohol or sedative-hypnotic abuse, neuropsychiatric abnormalities, and poorer outcome; more frequently associated with cortisol nonsuppression; and less likely to respond adequately to lithium but perhaps more likely to respond to ECT or anticonvulsants. **Conclusions:** Substantial evidence suggests that dysphoric mania may be a distinct affective state. Contrary evidence, however, suggests that dysphoric mania may be a form of typical mania, a stage-related or severe form of mania, or a transitional state between mania and depression. Because the evidence may be inconsistent because of varying definitions of dysphoric mania among studies, the authors propose preliminary operational diagnostic criteria for the future study of dysphoric mania.

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Mania and depression are often viewed as polar opposites. However, since Emil Kraepelin first described mixed states of manic-depressive insanity (1), it has been known that some patients with acute mania or hypomania simultaneously experience prominent depressive symptoms (1-28). Considerable ambiguity (27) still surrounds this condition, most commonly called dysphoric or mixed mania. For instance, dysphoric mania has been described as a distinct affective

state distinguishable from nondysphoric mania (1, 2, 7-9, 11, 13-26), as a form of typical mania (4, 6, 10), as a stage-related or particularly severe form of mania (5, 24), and as a transitional state between mania and depression (1, 7-9, 11, 12, 29-32). Moreover, the relationship of dysphoric mania to other affective states, such as agitated or mixed depression (32-35), rapid cycling and ultra-rapid cycling (7, 24, 36, 37), delirious mania (3, 4, 15), and the affective lability of borderline personality disorder (38-40), remains unclear.

Undoubtedly, much of the ambiguity surrounding dysphoric mania is due to the lack of widely accepted, empirically based operational diagnostic criteria for the disorder. Although most psychiatric classifications recognize the existence of mixed forms of bipolar disorder, they do not provide separate operational criteria for dysphoric or mixed mania (27), referring instead to different combinations of the criteria for mania and depression and specifying that manic and depressive symptoms either occur together (41), alternate rapidly (42), or occur together and alternate rapidly (43). Thus, DSM-III-R defines bipolar disorder, mixed, by two criteria: 1) current or most recent episode, which involves the "full symptomatic picture of both manic

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and major depressive episodes . . . intermixed or rapidly alternating every few days" and 2) prominent depressive symptoms lasting "at least a full day." Only the Vienna Research Criteria (42) provide specific operational diagnostic criteria for stable and unstable "mixed states." However, these criteria stress rapid change or fluctuation between manic and depressive symptoms—and less so the simultaneous occurrence of manic and depressive symptoms—without specifying the time periods within which the changes may occur. Indeed, most diagnostic criteria for mixed bipolar illness—Research Diagnostic Criteria (RDC), *DSM-III-R*, and the Vienna Research Criteria—do not distinguish clearly between dysphoric mania (mania accompanied by depressive symptoms) and ultra-rapid cycling (rapid alternations between mania and depression)—two conditions that may be distinguishable clinically (7, 24).

Given the lack of uniform operational criteria for dysphoric mania, this condition can be defined in broad, intermediate, or narrow terms: 1) mania or hypomania accompanied by any depressive symptom (broad), 2) mania or hypomania accompanied by several depressive symptoms (intermediate), and 3) mania accompanied by full-scale or syndromal major depression (narrow). Of these definitions, the broad one is probably not useful because many patients with acute mania simultaneously display at least some degree of depressed mood (1–4, 6, 10, 22, 24, 27). Therefore, we elected to review studies of dysphoric mania defined according to the intermediate or narrow definitions; we applied these definitions to studies examining dysphoric mania or hypomania, mixed mania, mixed states, and severe mania in patients with bipolar disorder. Studies apparently examining dysphoric mania or hypomania according to our intermediate or narrow definitions were then analyzed with regard to clinical characteristics, prevalence, demographic features, course of illness, outcome, family history, associated conditions, biological tests, and response to biological treatment.

CLINICAL CHARACTERISTICS: CLASSIC AND MODERN STUDIES

In the third century, according to Davidson (44), Aretaeus of Cappadocia observed that although some manic patients were "cheerful and like to play," others were "passionate and destructive." Robertson (45), in 1890, advocated dividing mania into "hilarious" and "furious" types. Kraepelin (1) described six types of mixed states based on different combinations of manic or depressive mood, activity, and thought (27). These states included depressive or anxious mania, excited or agitated depression, mania with poverty of thought, manic stupor, depression with flight of ideas, and inhibited mania. Of these six states, depressive or anxious mania—defined by depressed mood, manic activity, and manic thought—probably most closely resembles the definition of dysphoric mania used in this review.

Kraepelin described these patients as "anxiously despairing," greatly restless with "a wholly senseless pressure of activity," excited, and distractable, with flight of ideas and "ideas of sin and persecution."

Modern studies have generally defined dysphoric or mixed mania as mania accompanied by prominent depressive symptoms (table 1). Although most modern studies used standardized operational diagnostic criteria to define mania (e.g., RDC or *DSM-III*), they varied considerably in their definition of prominent depressive symptoms. For instance, several authors (3, 14, 26, 28) used a narrow definition of dysphoric or mixed mania, requiring that a *full* depressive syndrome co-occur with a full manic syndrome for a certain period of time. Most commonly, an intermediate definition was used, requiring only that several or substantial depressive features be present. The latter was usually determined when the patient achieved a certain score on specific depression rating instruments while acutely manic (e.g., a depression index score on the Manic-State Rating Scale [46] greater than or equal to 5 [6] or 8 [23], a depressive symptom cluster on the Kupfer-Detre System [47] greater than 18 [7–9], or a Hamilton Rating Scale for Depression [48] score greater than 7 [22] or 15 [15–18, 24]). Finally, some authors included mania with mild depression (22) and hypomania with prominent depression (6, 11, 39) as forms of dysphoric mania, and others included major depression with prominent agitation as a mixed bipolar state distinct from mixed mania (32, 35).

Many modern studies provided clinical descriptions of dysphoric mania. Patients were described as displaying a wide range and varied combinations of affective, cognitive, behavioral, and neurovegetative symptoms. Indeed, several authors remarked that the hallmark of dysphoric mania was variability or lability in mood and psychomotor activity (3, 4, 7, 12, 13, 24) or a "pleomorphic" or "chameleon-like" presentation with "innumerable combinations" of often contrasting symptoms (1, 2, 7–9, 26). In a study of 14 episodes of mixed manic-depressive psychosis in 10 patients, Winokur et al. (3) observed depression, euphoria, lability, irritability, distractibility, and greater psychomotor activity in all 14 episodes. Insomnia, pressure of speech, hostility, decreased sexual interest, grandiosity, and disorientation were seen in most episodes; suicidal threats or attempts, flight of ideas, increased alcohol intake, and anxiety attacks were also prominent.

Dysphoric mania appeared to be frequently accompanied by psychotic symptoms (often depressive or mood-incongruent) (1–3, 5, 7–9, 11–14, 20, 26, 28). In general, however, the overall incidence of psychosis did not differ between patients with dysphoric and nondysphoric mania (16, 26). Symptoms seen in delirious mania, such as incoherence and disorientation, were also frequently reported (3, 5, 15). Secunda et al. (15), for instance, found that patients with mixed mania displayed greater degrees of cognitive impairment than patients with nonmixed mania. Several studies suggested that patients with dysphoric mania were

TABLE 1. Studies of Dysphoric or Mixed Mania or Hypomania

Study	Definition ^a	N ^b	Prevalence of Dysphoric Mania		Female Patients With Dysphoric Mania (%)	Course	Treatment Response
			N	%			
Winokur et al. (3), 1969	Narrow	61	10	16	90 ^c	Episodes of dysphoric and nondysphoric mania of similar duration (8 weeks)	— ^d
Kotin et al. (4), 1972	Intermediate	20	13	65 ^e	— ^d	— ^d	One patient responded to lithium alone and one responded to lithium plus neuroleptic
Carlson et al. (5), 1973	Stage III ^f	20	14	70	— ^d	Patients with stage II and stage III mania had similar long-term outcomes	Patients with stage II and stage III mania had similar responses to acute and prophylactic lithium
Murphy et al. (6), 1974	Intermediate	30	17	57	65	— ^d	Nine of 12 euphoric-grandiose patients responded to lithium compared with none of three paranoid-destructive patients ($p < 0.01$) ^g
Himmelhoch et al. (7), 1976	Intermediate	84	26	31	— ^d	— ^d	11 (42%) of 26 patients with dysphoric mania responded to drug treatment compared with 47 (81%) of 58 patients with nondysphoric mania ($p < 0.001$); follow-up ranged from 9 months to 5 years
Nunn (11), 1979	Intermediate	112	40	36	60 ^h	— ^d	— ^d
Akiskal et al. (12), 1979	— ^d	60	15	25	— ^d	— ^d	One patient responded to lithium alone
Krishnan et al. (13), 1983	Intermediate	10	— ^d	— ^d	90	— ^d	— ^d
Evans et al. (14), 1983	Narrow	10	7	70	57	— ^d	Two of seven patients responded to lithium, one to lithium plus neuroleptic, and one to ECT
Secunda et al. (15, 18), 1985–1987	Intermediate	19	8	42	— ^d	— ^d	Two of seven patients with dysphoric mania responded to lithium compared with 10 of 11 patients with nondysphoric mania ($p = 0.01$) ^d
Keller et al. (19–21), 1985–1988	Intermediate	130	7 ⁱ	5	— ^d	Episodes of dysphoric mania of significantly longer duration (14 weeks) than episodes of nondysphoric mania (5 weeks) and major depression (9 weeks) ($p < 0.03$)	— ^d
Prien et al. (22), 1988	Broad and intermediate	103	23 ^j	22	41 (broad)	Patients with dysphoric mania had significantly higher relapse rate than patients with nondysphoric mania	25 (36%) of 69 patients with mild to severe dysphoric mania responded to lithium, neuroleptic, lithium plus neuroleptic, or lithium plus antidepressant compared with 20 (59%) of 34 patients with pure mania ($p < 0.001$)
Cohen et al. (23), 1988	Intermediate	23	8	35	— ^d	Patients with dysphoric mania had significantly poorer outcome at hospital discharge than patients with nondysphoric mania despite similar treatments	— ^d
Post et al. (24), 1989	Intermediate	48	22	46	— ^d	Patients with dysphoric mania had significantly more hospitalizations (mostly for depression) despite fewer mood episodes (less rapid cycling) than nondysphoric mania patients	— ^d

TABLE 1 (continued)

Study	Definition ^a	N ^b	Prevalence of Dysphoric Mania		Female Patients With Dysphoric Mania (%)	Course	Treatment Response
			N	%			
Tohen et al. (25), 1990	Intermediate	75	38	51	— ^d	Patients with dysphoric mania relapsed significantly sooner than those with nondysphoric mania	— ^d
Dell'Osso et al. (26), 1991	Narrow	108	49	45	— ^k	Once dysphoric mania occurred, subsequent episodes tended to be mixed	— ^d
Strakowski et al. (28), 1992	Narrow	41	8	20	— ^l	No differences in outcome between patients with dysphoric and nondysphoric mania at hospital discharge	— ^d

^aBroad=mania or hypomania accompanied by mild depression. Intermediate=mania or hypomania accompanied by prominent depressive symptoms. Narrow=mania or hypomania accompanied by full-scale or syndromal major depression. Stage II=moderately severe mania, characterized predominantly by anger and irritability. Stage III=mania at peak severity, characterized by extreme dysphoria, desperation, severe panic, hopelessness.

^bNumber of patients with acute mania or hypomania studied.

^c63% of all patients with mania were female.

^dInformation not provided.

^e62% of the patients in the nondysphoric group were female.

^f14 of 20 patients displayed stage III mania.

^gParanoid-destructive group had higher depression scores than euphoric-grandiose group; higher depression scores correlated with favorable lithium response, but not significantly. Rate of lithium response for patients with high depression scores not ascertained.

^h64% of the patients in the nondysphoric group were female.

ⁱAn additional 60 patients displayed cycling between mania or hypomania and depression.

^jAn additional 46 patients had mixed mania with mild depression.

^kAll of the patients in the study were women.

^lSame percentage of females in dysphoric and nondysphoric groups.

more severely ill than nondysphoric patients (5, 6, 22, 23), but the range of severity was wide and overlapped substantially with nondysphoric patients (7, 15–18, 22, 23, 26). Finally, suicidal ideation was frequently observed (3, 4), and the combination of manic and depressive features was noted to constitute a particularly uncomfortable and driven state with a high risk for suicide (49, 50).

In summary, dysphoric mania appears to cover a wide range of symptoms and severity and may include the most severely ill patients with bipolar disorder. The considerable variation in the clinical descriptions of patients, therefore, may be due not only to the lack of standardized operational criteria and differences in patient populations between centers (table 1) but also to the variable nature of the condition.

PREVALENCE OF DYSPHORIC MANIA

Earlier investigators, including Kraepelin in 1921 (1) and Winokur et al. 1969 (3), believed that mixed states are uncommon. Indeed, Silverman (51) wrote that mixed states are so infrequent that a conceptual model of manic-depressive illness need not explain them. However, the more recent studies summarized in table 1 (3–7, 11, 12, 14–26, 28) reported rates of mixed states among acutely manic patients with bipolar disorder ranging from 5% (19–21) to 70% (14). This wide

variation in prevalence across different studies is likely due in part to variations in the criteria used to define dysphoric mania. Indeed, depending on definition—typically of the degree of depression—rates can vary within the same study (22). Nevertheless, despite the wide variation in definition and prevalence across these studies, the overall mean prevalence of 31% (305 of 981 patients) suggests that dysphoric mania is more common than once believed.

DEMOGRAPHIC FEATURES, COURSE OF ILLNESS, AND OUTCOME

Studies comparing demographic and other clinical features of patients with dysphoric versus nondysphoric mania show many inconsistencies. Some studies (3, 6, 13, 14) found that a higher percentage of patients with dysphoric mania than patients with pure mania were female. Most studies reported that patients with mixed and nonmixed mania had similar ages. Himmelhoch and Garfinkel (9), however, noted that adolescents with mania frequently presented with a mixed picture. Also, patients with dysphoric mania have been shown to have a younger (11, 24), similar (26), and older (28) age at onset of illness as well as a longer (11, 26) and similar (24) overall duration of illness compared with patients with pure mania. Regarding episode duration, dysphoric manias have been reported to

be shorter than (36), equal to (3), and longer than (19–21, 26) pure manias.

Studies also varied in the number and type of previous affective episodes experienced by patients with dysphoric mania. Compared with patients with pure mania, patients with dysphoric mania have been found to have more previous episodes (11), similar numbers of previous episodes (22), and fewer previous episodes but more psychiatric hospitalizations (24). Several authors reported that patients with dysphoric mania have higher rates of depression than patients with nonmixed mania early in the course of their illness—with higher rates of premorbid depressive temperament (26), greater likelihood of beginning their illness with a depressive episode (11), and greater numbers of hospitalizations for depressive episodes (24). Onset of dysphoric mania relative to other episodes was also variable. Although some authors (1, 26) reported that mixed manias tend to occur for the first time later in the course of illness, others noted that a substantial proportion of patients with bipolar disorder experience mixed mania as their initial episode (9, 26, 28, 52, 53). Moreover, Dell'Osso et al. (26) found that once a patient experienced a mixed mania, subsequent episodes tended to be mixed.

Regarding outcome, Kraepelin (1) noted that “the course of mixed states occurring as independent attacks appears in general to be lingering; they might be regarded as unfavorable forms of manic-depressive insanity.” Despite some inconsistencies (5, 28), modern studies generally support Kraepelin's observation that patients with dysphoric mania exhibit a poorer prognosis—acutely and over the long-term—than patients with pure mania. Dysphoric patients have been shown to take longer to recover from an acute episode (19–21), to do less well on short-term (23) and long-term follow-up (7), and to be more likely to relapse (22) or to relapse sooner (25) after recovery than nondysphoric patients.

In summary, data on demographic features and course of illness are inconclusive but suggest that dysphoric mania is not limited to any group of patients or stage of illness. However, episodes of dysphoric mania may have poorer short-term and long-term outcomes than pure manic episodes.

FAMILY HISTORY

We found only one study of the families of individuals with dysphoric mania. Using the Family History Research Diagnostic Criteria (54), Dell'Osso et al. (26) compared the first-degree relatives of 49 patients with mixed mania with those of 59 patients with pure bipolar disorder. They found no differences between the two groups in familial affective loading or in family history of suicide or suicide attempts. However, depressive disorders were more common in the families of patients with mixed mania and bipolar disorders were more common in the families of patients with nonmixed mania.

ASSOCIATED CONDITIONS

Few studies have assessed psychiatric or medical conditions associated with dysphoric mania. Winokur et al. (3) noted that of 14 mixed manic-depressive episodes, two occurred postpartum and two were immediately preceded by psychologically stressful events (e.g., the death of a spouse). Dell'Osso's group (26) and Swann et al. (55), however, found that patients with mixed and nonmixed mania did not differ regarding the frequency of antecedent stressful events.

Himmelhoch et al. (7) found that significantly more patients with mixed mania than patients with nonmixed mania had alcohol and substance abuse. They suggested two hypotheses to explain this finding: either dysphoria leads to substance abuse or substance abuse leads to dysphoria. In the first case, the higher rate of substance abuse would presumably reflect an attempt by patients to treat the intense discomfort of dysphoric mania. In the second, the effects of drug abuse—intoxication and withdrawal—might adversely affect the natural course of a manic episode, converting a pure euphoric state into a dysphoric state.

In a follow-up study, Himmelhoch and Garfinkel (9) reported that 45 (71%) of 63 patients with mixed mania, compared with seven (12%) of 58 patients with nonmixed mania ($p < 0.001$), had concomitant neuropsychiatric abnormalities. These neuropsychiatric factors included paroxysmal EEG abnormalities ($N=20$), alcohol and drug abuse ($N=12$), developmental disorders ($N=8$), migraine ($N=6$), seizure disorders ($N=5$), substantial head injuries ($N=4$), and neurological illnesses ($N=2$). Of note, only one of the 45 patients with mixed mania and an associated neuropsychiatric abnormality responded to lithium. In contrast, Strakowski et al. (28) reported that eight patients with mixed bipolar disorder showed no differences from 33 patients with nonmixed bipolar disorder in medical and psychiatric comorbidity.

Very few data are available regarding the relationship of dysphoric mania to other mixed states. For instance, we were unable to locate any studies comparing a group of rigorously diagnosed patients with dysphoric mania with a group of patients with agitated depression or delirious mania. Nevertheless, Himmelhoch's group (32) reported that agitated psychotic depression associated with hypomania or mania was a rare syndrome. In addition, Tandon et al. (34) concluded that patients with mixed depression could be distinguished biochemically from those with mixed mania.

Two studies systematically assessing rapid cycling among patients with dysphoric mania (7, 24) suggested that the two conditions may not be related. Himmelhoch et al. (7) reported that patients with mixed and nonmixed mania showed similar rates of “mood circularity” (defined as episodes of mania and depression *not* separated by periods longer than 2 months). Post et al. (24) reported that patients with dysphoric mania were significantly less likely to exhibit rapid cycling in the year before index admission than were patients with

pure mania. Also, although patients with rapid cycling and patients with nonrapid cycling showed equal peak manic severity at index episode, the patients with rapid cycling showed significantly less dysphoria, anxiety, and psychosis during mania. Patients with rapid cycling, however, have been reported to experience mixed episodes (8, 36). Also, dysphoric mania and rapid cycling may share a greater prevalence among female patients, poorer response to lithium, possible induction by antidepressants, and better response to anticonvulsants (37). Further, the rapid mood shifts described in patients with dysphoric or mixed mania (3, 7-9, 24) may resemble the 24-hour mood shifts described in some patients with bipolar disorder who experienced ultra-rapid cycling (56, 57). However, the relationship between dysphoric mania and ultra-rapid cycling also remains unclear.

Finally, little is known about the relationship between dysphoric mania and personality disorders. Although we were unable to locate any studies using structured interviews to assess this relationship, mixed states (including dysphoric hypomania and ultra-rapid cycling) have sometimes been seen as expressions of borderline personality disorder, largely because these conditions share phenomenological similarities, a higher rate in females, and poor response to lithium (38-40). Akiskal's group, however, argued that many individuals diagnosed with borderline psychopathology may in fact have subtle or "soft" forms of bipolar disorder, including cyclothymia with brief mixed states (38, 39) and prolonged mixed states (e.g., chronic dysphoric hypomania) (40). Although Akiskal's group noted that the abrupt mood shifts in these individuals may give rise to serious characterological disturbances, they reported that psychotherapy is generally ineffective in the absence of adequate pharmacotherapy of the underlying affective instability (38-40).

STUDIES OF BIOLOGICAL TESTS

Studies of the biology of dysphoric mania have primarily examined hypothalamic-pituitary-adrenal (HPA) axis function and plasma or cerebrospinal fluid (CSF) concentrations of neurotransmitters or their metabolites (27). Reports of cortisol function in manic patients in general are inconsistent (14, 27, 58, 59). Some studies (14, 58, 59) found normal cortisol suppression on the dexamethasone suppression test (DST), but others (60-62) found rates of nonsuppression on the DST comparable to those in depression. Nevertheless, several small studies suggested that patients with dysphoric mania may be more likely than patients with pure mania to show DST non-suppression (13, 14, 27). For example, Evans and Nemeroff (14) reported that seven patients with mixed mania (meeting *DSM-III* criteria for both manic and depressive episodes) were DST non-suppressors and that three patients with pure mania were normal suppressors. Five of the patients with mixed mania showed normalization of suppression

when retested after successful treatment. Similarly, of 10 consecutive patients with simultaneous manic and depressive symptoms studied by Krishnan et al. (13), all manifested abnormal cortisol suppression after the DST. Swann et al. (63) recently reported that plasma and CSF cortisol were elevated in patients with mixed mania to an extent similar to or greater than that in agitated depressed patients but were normal in patients with nonmixed mania. In contrast, although one of the studies finding elevated cortisol nonsuppression rates in manic patients (61) did not differentiate between dysphoric and pure mania, one specified that the manic patients studied were not simultaneously depressed (60), while another (62) reported cortisol nonsuppression in five of seven patients with mixed mania and three of nine patients with pure mania.

In studies of neurotransmitter metabolism, Post et al. (24) found that acutely manic patients had significantly higher CSF norepinephrine concentrations than did depressed and euthymic patients and that the degree of norepinephrine elevation correlated with the degree of manic dysphoria, anger, and anxiety. Swann et al. (64) reported similar results with CSF 3-methoxy-4-hydroxyphenylglycol and urinary excretion of norepinephrine and its metabolites, finding no differences between patients with mixed and pure mania.

Regarding other neurotransmitter systems, Tandon et al. (34) found that CSF concentrations of homovanillic acid and 5-hydroxyindoleacetic acid in patients with *DSM-III-R* mixed bipolar disorder were intermediate between those in patients with pure mania and those in patients with major depression; the highest concentrations occurred in the patients with pure mania. Moreover, the mixed group could be subdivided into two groups—mixed manic and mixed depressive. The metabolite levels of these two groups resembled those of the pure manic and pure depressive groups, respectively. The authors concluded that mixed affective states do not exist as a distinct homogeneous entity but are composed of two subgroups representing mixed forms of manic and major depressive states, respectively.

RESPONSE TO BIOLOGICAL TREATMENT

Lithium

We know of no placebo-controlled studies of lithium in the treatment of acute dysphoric mania. However, case reports and case series report the successful treatment of patients with dysphoric mania with lithium alone (4, 5, 12, 14, 52) or in combination with antipsychotics (4, 5, 14) or clonazepam (65). For example, Evans and Nemeroff (14) reported that of seven patients meeting *DSM-III* criteria for mixed bipolar disorder, six responded to lithium alone ($N=2$) or in combination with thiothixene ($N=4$), while the seventh responded only when ECT was administered. Carlson and Goodwin (5) reported that all 14 of the patients they studied with stage III mania (severe mania marked

by prominent dysphoric mood) showed an acute anti-manic response to lithium—sometimes in conjunction with antipsychotics. Many studies, however, suggest that acute dysphoric mania responds less well or less quickly to lithium than does pure mania (6, 7, 9, 15–18, 22, 23). These studies have methodological limitations: all were uncontrolled, some did not clearly specify that lithium was used but only implied that it was, and most used concomitant psychotropics. Nevertheless, if the results of these studies are pooled, 38 (36%) of 105 patients with dysphoric or mixed mania but 86 (75%) of 115 nondysphoric patients responded well to lithium over treatment periods ranging from 24 days to 5 years ($p < 0.001$) (6, 7, 15–18, 22). Moreover, Himmelhoch and Garfinkel (9) reported that of 46 lithium-resistant patients with bipolar disorder, 37 (80%) had mixed mania. These results have led a number of investigators to conclude that dysphoric mania is less responsive to lithium than nondysphoric mania. However, it has been suggested that dysphoric patients may simply need a longer period of treatment before showing an adequate response (15–18).

Long-term studies suggest that prophylactic treatment with lithium is less effective in patients with dysphoric mania than in those with pure mania. Himmelhoch et al. (7) found that patients with mixed mania showed a poorer response to psychopharmacological treatment than patients with nonmixed mania at follow-up ranging from 9 months to 5 years. We know of only one controlled prophylactic drug treatment study of dysphoric mania: Prien et al. (22) found that patients with an index mixed manic episode treated with lithium or lithium plus imipramine for a 2-year period were significantly more likely to experience a recurrence than similarly treated patients with nonmixed manic index episodes. In contrast, in an open retrospective study of 88 patients with manic-depressive psychosis and recurrent depression who had received lithium treatment for at least 1 year, Baastrup and Schou (52) found that 24 (86%) of 28 patients who had experienced mixed episodes during the course of their illness appeared to display a beneficial prophylactic response.

Anticonvulsants

Several studies indicate that patients with dysphoric mania may respond favorably to the anticonvulsant agents carbamazepine and valproate. In a placebo-controlled study of carbamazepine in 19 patients with acute mania, Post et al. (66) found a trend for patients with high levels of dysphoria to respond better than nondysphoric patients. Hayes (67) found that all 12 patients with “mixed bipolar disorders” (the diagnostic criteria were not specified) in an open study of valproate showed improvement in affective symptoms and that six also showed improvement in psychotic symptoms. McFarland et al. (68) found that five of six elderly patients with bipolar disorder in an open-label trial of valproate displayed moderate to marked improvement, including three patients with mixed mania. Calabrese

and Delucchi (36) found that valproate was highly effective in the acute and prophylactic treatment of both manic and mixed episodes (defined by *DSM-III-R* criteria) but less effective in the acute and long-term treatment of depressive episodes in an open, prospective study of valproate in 55 patients with rapid-cycling bipolar disorder. In a follow-up study with 78 patients, Calabrese et al. (69) reported that 54% of patients with mania, 87% of those with mixed states, and 19% of those with depression showed marked acute responses to valproate and that 72% of manic patients, 94% of mixed state patients, and 33% of depressed patients showed marked prophylactic responses. In a controlled comparison of lithium versus valproate in 27 patients with acute mania, Freeman et al. (70) and Clothier et al. (71) found that, unlike the response to lithium, favorable response to valproate was associated with higher pretreatment depression scores (measured by depression factor scores on the Schedule for Affective Disorders and Schizophrenia—Change Version [SADS-C] [72]). Specifically, of 14 patients receiving valproate, all four with mixed mania (defined as *DSM-III-R* mania and a SADS-C depression score greater than 30) responded, compared with five of 10 patients with nonmixed mania.

In contrast, although 21 (46%) of their 46 lithium-resistant patients (80% of whom had mixed mania) responded to “anticonvulsant based therapy,” Himmelhoch and Garfinkel (9) noted that eight of nine patients with “pure presentations” also responded to anticonvulsant treatments. Finally, in a placebo-controlled study of valproate in 36 patients with acute mania (73), our group found that favorable antimanic response to valproate was not associated with levels of depression or dysphoria as measured by individual and composite scores on the Brief Psychiatric Rating Scale (74).

Antipsychotics

We found no controlled studies of antipsychotics in the treatment of dysphoric mania. However, in an open survey of the efficacy of the atypical antipsychotic clozapine in patients with psychotic mood disorders (75), we observed that, of seven patients with bipolar disorder characterized by dysphoric mania, psychosis, and chronic disability refractory to lithium, standard antipsychotics, and anticonvulsants, all showed marked short- and long-term symptomatic and functional improvement in response to clozapine treatment.

Antidepressants

We located only one controlled study of antidepressant agents in the treatment of dysphoric mania. Comparing lithium alone, imipramine alone, and lithium in combination with imipramine in the treatment of 25 patients with mixed mania (16 of whom had mania with mild depression and nine of whom had mania with moderate or severe depression), Prien et al. (22) found that five of eight patients treated with lithium,

all of seven treated with imipramine, and nine of 10 treated with the combination experienced a recurrence. Imipramine treatment, in short, was associated with a greater risk of recurrence. Consistent with these findings, other authors have noted that antidepressants may induce or exacerbate mixed mania or similar mixed states. Akiskal and Mallya (38, 39) reported that 25 patients referred for treatment-resistant depression displayed subacute or chronic mixed states apparently induced by tricyclic antidepressants. These states were characterized by unrelenting dysphoria, severe agitation, refractory anxiety, unendurable sexual excitement, intractable insomnia, suicidal obsessions and impulses, and histrionic demeanor. They improved with antidepressant discontinuation and initiation of lithium or carbamazepine. Koukopoulos et al. (35) found that 45 patients with bipolar disorder suffering from a "mixed depressive syndrome" who met *DSM-III-R* criteria for major depression but not for mania deteriorated when treated with antidepressants—experiencing increased agitation, insomnia, and, in some, suicidal impulses. Patients responded to low-dose neuroleptics, lithium, anticonvulsants, and ECT. Of note, it remains unclear whether mixed manias are more likely to deteriorate than nonmixed manias when exposed to antidepressants.

ECT

Case reports have described the successful treatment of dysphoric mania with ECT (2, 14). In a randomized comparison of ECT versus lithium in 34 patients with acute mania, Small et al. (76) found that patients receiving ECT improved more during the first 8 weeks of treatment than patients receiving lithium. This was especially true of patients with "mixed symptoms of mania and depression and/or extreme manic behavior." Indeed, Small et al. reported that baseline ratings of depression during mania were the strongest predictor of clinical outcome at 8 weeks and that depressive symptoms worsened during lithium treatment but not with ECT—leading the authors to suggest that ECT was more likely than lithium to prevent the "switch over to depression that commonly follows a manic episode."

In summary, a substantial amount of data suggest that lithium may be less effective in the short- and long-term treatment of dysphoric mania than it is in pure mania. Although anticonvulsants and ECT may be more effective in these patients, the studies supporting these treatments are difficult to interpret due to numerous methodological limitations, including variable definitions of dysphoric mania (table 1). Importantly, controlled trials directly comparing lithium, different anticonvulsants, and ECT in adequate numbers of patients with well-defined dysphoric and nondysphoric mania have not yet been conducted. Therefore, whether anticonvulsants and ECT are more effective than lithium in dysphoric mania and whether they are more effective in dysphoric than nondysphoric mania remain

to be definitively proven. It is particularly noteworthy, however, that antidepressants may make these patients worse.

DISCUSSION

Although long recognized, dysphoric or mixed mania remains an understudied and incompletely understood condition. The consensus of the studies reviewed in this paper is that dysphoric mania may be different from nondysphoric mania. Phenomenologic studies suggest that mania accompanied by substantial depression may be more variable, more likely to be associated with depressive delusions and suicidality, and sometimes more severe than pure mania. Studies of demographics, course of illness, and family history suggest that, compared with nondepressed manic patients, dysphorically manic patients may be more likely to be female; to have an earlier age of onset and a longer duration of illness; to have higher rates of depression in their early histories and families; and to have protracted episodes, poorer short- and long-term outcome, and a higher likelihood of recurrence. Biological studies suggest that dysphoric mania may be more frequently associated with non-suppression of plasma cortisol after dexamethasone administration than pure mania. Finally, treatment response studies suggest that, compared with nondysphoric mania, dysphoric mania may be less likely to respond to lithium but more likely to respond to anticonvulsants or ECT.

But what exactly is dysphoric mania? Investigators have variously speculated that dysphoric mania might represent a stage-related or severe form of mania, a transitional state between manic and depressive episodes, a form of typical mania, as well as a distinct affective state. Indeed, different studies suggest that dysphoric mania may be all of these things—in different patients, or in the same patient at different times.

Is dysphoric mania simply severe mania? In their study documenting three stages of mania, Carlson and Goodwin (5) prospectively observed that manic episodes become progressively more severe and more dysphoric over time. In addition, as noted, patients with the most severe (stage III) mania do not differ regarding outcome and lithium response from those with less severe (stage II) mania. The notion that dysphoric mania is a stage-related form of mania—mania at its peak severity—is further supported by findings that depression, anger, and hostility during mania correlate positively with the overall severity of the manic episode (5, 6, 24). However, viewing dysphoric mania simply as severe mania does not account for two observations: many studies (7, 15–18, 22, 23, 26) report that the presence or degree of depression during mania does *not* correlate with ratings of overall manic severity and, perhaps more importantly, patients have been reported to experience dysphoric hypomania, or hypomania associated with prominent depression (6, 11, 39). Thus, although dysphoric mania may include the most severely

ill patients, a wide range of severity in manic symptoms can be present.

Does dysphoric mania represent a transitional state—the so-called switch process between mania and depression or depression and mania? Himmelhoch et al. (7–9) proposed that mixed affective states represent patients getting “trapped” in the switch state from depression to mania. Sitaram et al. (77), in a study of switches into and out of mania in 75 patients with bipolar disorder, found that 35 patients displayed 89 “rapid” switches (occurring in 24 hours or less) and 14 patients displayed 27 “slow” switches (occurring over periods of two to six days)—suggesting that the switch process may sometimes be protracted. This formulation is consistent with the continuum model of bipolar disorder (78), which posits that mania and depression are physiologically similar states that may be quantitatively different and exist along a continuum of severity where depression represents mild to moderate illness, mania represents severe illness, and mixed states represent transitional forms. However, available data indicate that the phenomenology of the switch process is variable. In their longitudinal study of the switch process, Bunney et al. (29–31) found that the most severe degree of depression occurring during mania seemed to occur in patients with “normal” transitions from depression to mania—after the switch had occurred and the patient had become acutely manic. These findings, combined with observations that patients can experience isolated mixed episodes—either as an initial episode or later in the course of illness without preceding or subsequent mood episodes—support the notion that at least some dysphoric manias are not transitional states. Indeed, Berner’s group (42) has identified stable and unstable mixed states, and Cassano et al. (40) have distinguished “pure mixed states” in which the “entire episode is one of mixed symptomatology” and which can be chronic, from the “typically short-lived transitional phenomena between manic and retarded depressive states.”

Is dysphoric mania a distinct state rather than a stage in typical mania? Although many manic patients experience some degree of depressed mood (1–4, 6, 10, 22, 24, 27), the depression is often fleeting or mild (3). The findings of this review suggest that manic patients with prominent or severe depression may be different from those with mild depression. How, then, could dysphoric mania occur as a distinct state? One possibility is that dysphoric mania is a heterogeneous condition with numerous etiologies—reflecting, for example, mixed heredities (the inheritance of two or more illnesses such as bipolar disorder and unipolar depression) or the possibility that mania can be modified by secondary factors (e.g., alcohol or substance abuse, neurological abnormalities, premorbid temperament, personality disorder, or antidepressant treatment) (7–9, 26, 38, 39). Alternatively, adhering to a bipolar model, if the physiological abnormalities causing mania and depression are truly different, or even opposites, dysphoric mania might represent these abnormalities occurring simultaneously, perhaps in different regions of the central nerv-

ous system (e.g., HPA axis overactivity in the hypothalamus and noradrenergic overactivity in the limbic system). This possibility is supported by findings of HPA axis and norepinephrine overactivity in dysphoric mania. Or, taking the “permissive hypothesis” of Prange et al. (79) one step farther, we could posit that perhaps some central abnormality needs to be present in order for the abnormalities underlying mania and depression to occur simultaneously. Yet another possibility is that dysphoric mania is due to a third distinct pathophysiological abnormality.

Recognizing dysphoric mania as a separate affective state may have important clinical and theoretical implications. First, dysphoric mania may be more common than initially thought—possibly even more common than pure mania (4, 6, 22). Indeed, in reviewing studies of the phenomenology of mania conducted during the past 70 years, Goodwin and Jamison (27) concluded that depression and irritability were more common than euphoria in mania. Second, because dysphoric mania is varied in its presentation, it could be confused with a number of other psychiatric conditions, including major depression, agitated depression, atypical depression, delusional depression, ultra-fast cycling, delirious mania, schizophrenia, panic disorder, alcohol and substance abuse, personality disorder, and organic mental disorder (3, 7–9, 12, 15, 27, 32–40). It would be important to distinguish dysphoric mania from these other conditions so that treatments that could potentially worsen dysphoric mania (e.g., antidepressants) would be avoided, while treatments that might be particularly beneficial (e.g., anticonvulsants and ECT) would not go unused and, conversely, so that treatments which might worsen other conditions (e.g., ECT in personality disorder or organic mental disorder) would not be inadvertently misused. Third, certain patients with bipolar disorder might have a greater risk of developing mixed states. These patients might include adolescents or women and those with associated alcohol and substance abuse, high rates of depression in their personal and family histories, neuropsychiatric abnormalities, or a history of treatment with antidepressants. Finally, dysphoric mania might display a more malignant course of illness and have a greater risk for suicide and poorer treatment outcome than typical bipolar disorder.

Theoretically, if dysphoric mania proved to be a separate affective state distinct from depression and mania rather than a stage-related or transitional state, it could be argued that triangular (80) or bidimensional (81) models of mood disorder, which recognize this possibility, may be more appropriate than bipolar or continuum models. Such models would also have to address the relationship among dysphoric mania, ultra-fast cycling, agitated or mixed depression, and other mixed states—disorders that might exist along a continuum of combined manic and depressive symptoms. Agitated depression would represent severe depression with mild mania, and dysphoric mania would represent severe depression with severe mania. Anxious depression, dys-

phoric hypomania, and ultra-fast cycling might represent transitional forms between the extremes of agitated depression and dysphoric mania of greater and lesser severity, respectively. Of note, Emrich (81) has proposed a bidimensional model of manic-depressive illness according to which mixed states are assumed to occur more frequently during the time between peak mania and peak depression but may themselves be of greater and lesser degrees of severity.

To determine whether dysphoric mania is a distinct entity and to test these various hypotheses, operational diagnostic criteria for dysphoric mania need to be developed and tested. Based on this review and on the conceptual definition of dysphoric mania as mania accompanied by prominent depression, we propose that dysphoric mania be defined operationally by the presence of three or more symptoms of major depression during a full manic or hypomanic episode by *DSM-III-R* criteria (appendix 1). We are specifying that three depressive symptoms be present to ensure that the patient displays prominent but not necessarily full syndromal depression. If two depressive symptoms are present, however, a diagnosis of probable dysphoric mania would be made. We propose further that the specific depressive symptoms include depressed mood; markedly diminished interest or pleasure in all, or almost all, activities; substantial weight gain or increase in appetite; hypersomnia; psychomotor retardation; fatigue or loss of energy; feelings of worthlessness or excessive or inappropriate guilt; feelings of helplessness or hopelessness; and recurrent thoughts of death, recurrent suicidal ideation, a suicide attempt or a specific plan for committing suicide. However, we do not include insomnia, reduced appetite, psychomotor agitation, or diminished ability to concentrate because of the difficulty in reliably determining if these symptoms are primarily manic or depressive. Finally, we also propose that patients with rapid cycling should not be classified as having dysphoric mania unless they have experienced three depressive symptoms while also experiencing a full manic or hypomanic syndrome. This would enable patients with rapid cycling to be classified as with and without dysphoric mania.

Systematic studies could compare patients meeting these criteria with patients with pure mania, pure depression, other potential mixed states (e.g., agitated depression, mania with mild depression, and ultra-fast cycling with pure mania), and personality disorder. Until this research is done, investigators and clinicians should be aware that dysphoric mania exists, that it may be more common than realized, that it may be confused with a variety of other psychiatric disorders, and that it may display an outcome and treatment response different from that of nondysphoric mania.

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APPENDIX 1. Operational Diagnostic Criteria for Dysphoric Mania or Hypomania

- I. A full manic or hypomanic syndrome by *DSM-III-R* criteria
- II. Simultaneous presence of at least three associated depressive symptoms from the following list (for a definite di-

agnosis of dysphoric mania or hypomania, three depressive symptoms are present; for a probable diagnosis of dysphoric mania or hypomania, two symptoms are present; for a possible diagnosis of dysphoric mania or hypomania, one symptom is present)

1. Depressed mood
2. Markedly diminished interest or pleasure in all, or almost all, activities
3. Substantial weight gain or increase in appetite
4. Hypersomnia
5. Psychomotor retardation
6. Fatigue or loss of energy
7. Feelings of worthlessness or excessive or inappropriate guilt
8. Feelings of helplessness or hopelessness
9. Recurrent thoughts of death, recurrent suicidal ideation, or a specific plan for committing suicide

Problems and Considerations in the Valid Assessment of Personality Disorders

J. Christopher Perry, M.P.H., M.D.

This article reviews evidence for the reliability and diagnostic concordance of structured-interview and self-report questionnaire methods for the diagnosis of personality disorders. The findings of nine studies that compared two or more axis II diagnostic instruments administered to the same groups of subjects are summarized. Across the eight studies with sufficient data, a summary of the overall diagnostic agreement between any two instruments yielded a low reliability (median kappa=0.25) for making individual personality disorder diagnoses. Diagnostic concordance was lower between self-report questionnaire and interview methods than between interview methods. Comparing dimensional scores of different methods did not appreciably improve the level of agreement. The author concludes that current methods for making personality disorder diagnoses have high reliability but yield diagnoses that are not significantly comparable across methods beyond chance, which is not scientifically acceptable. Sources for the disagreement include variance due to different raters, interview occasions, data sources (self-report versus observer report), information bases obtained, and instrument sensitivity to state effects (e.g., mood). Serious problems in assessment validity may also arise from the yes/no format, which, despite probes for confirmatory examples, may fail to distinguish adequately between sporadic occurrences and longstanding patterns. Efforts should be made to improve and demonstrate the validity of axis II diagnostic methods. One route to increasing validity is to improve the clinical interview, because personality patterns are best revealed by the recurring patterns one finds when taking a systematic history.

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Prior to the introduction of specific diagnostic criteria, the reliability of personality disorder diagnoses was low. A review of studies from the pre-DSM-III era demonstrated that the mean interrater reliability (kappa) for clinical diagnoses of personality disorders was 0.32 (1). With the introduction of criteria, in the DSM-III field trials the kappa for the presence of any axis II diagnosis was 0.61 in conjoint interviews and 0.54 when independent interviews were conducted (2). However, others (3) reported an overall kappa of 0.41 between independent interviews, with lower concordances for individual disorders (median kappa=0.23). Because low reliability constrains the validity of any assessment, these findings have highlighted the necessity

of adding some procedural guidelines to the nonsystematic clinical interview to improve reliability. The success of the Schedule for Affective Disorders and Schizophrenia/Research Diagnostic Criteria system (4, 5) in yielding reliable diagnoses encouraged the development of both structured-interview and self-report assessments of personality disorders, focusing on the DSM-III and DSM-III-R criteria. As this scientific endeavor has matured, a number of studies have compared different instruments used with the same groups of subjects. This report reviews how well these instruments agree when the same individuals are being diagnosed and discusses issues of assessment validity that are important for both research and clinical practice.

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DESCRIPTION OF DIAGNOSTIC INSTRUMENTS

Following is a brief description of the instruments that have been used in studies comparing the concordance of axis II diagnoses according to DSM-III or DSM-III-R criteria. This list omits instruments for which comparison studies were not found. Reich (6, 7) has reviewed these and other instruments as well.

The National Institute of Mental Health Diagnostic Interview Schedule (DIS) (8), devised for use in the Epidemiologic Catchment Area (ECA) study of *DSM-III* axis I disorders, assesses one axis II disorder, antisocial personality disorder. Each criterion is assessed by one or more questions without probes for examples. Robins et al. (8) reported that the interrater reliability for the antisocial personality diagnosis in a comparison of lay and psychiatrist interviewers was 0.63. Subsequently, the ECA study reported a median lifetime prevalence across its sites of 2.5% overall and 4.5% among the 24- to 44-year-old age group sampled (9).

The Personality Disorders Examination, devised by Loranger (10, 11), is a structured interview yielding 11 *DSM-III-R* personality disorder diagnoses; the 1988 version includes the two (self-defeating and sadistic) listed in the *DSM-III-R* appendix. The questions are organized by topic area rather than by diagnosis, giving the interview a natural flow from the patient's point of view. The current (1988) version includes a number of questions with probes asking for examples or anecdotes following a positive answer. A report on an earlier version (11) yielded high levels of agreement on all diagnoses and high interrater reliability for five diagnoses with sufficient base rates (median kappa=0.80, range=0.70–0.96). Interrater reliability of the dimensional scores for each disorder was very high (median intraclass correlation=0.97). Short-term retest reliability for four diagnoses with calculable kappa coefficients was moderately good (median kappa=0.49, range=0.37–0.56). Standage and Ladha (12) confirmed that overall interrater reliability was acceptable (median kappa=0.63, range=0.38–0.78). Pilkonis et al. (13) obtained an overall interrater reliability kappa of 0.79 for whether any personality disorder was present, and the 6-month retest stability of kappa was 0.52. Kappas for individual disorders were not reported.

The Structured Clinical Interview for *DSM-III-R* Personality Disorders (SCID-II) was devised by Spitzer et al. (14) as a companion to the SCID for axis I disorders. It covers the 11 axis II disorders plus self-defeating personality from the appendix to *DSM-III-R*. The questions are organized by diagnosis, so that all of the criteria for a disorder are assessed together, making it easy for the interviewer to assess one disorder at a time. Interviewers are encouraged to ask additional questions to clarify ambiguous responses, although clarifying questions are not specified. A recent version of the SCID-II uses a series of self-report questions which, if the answers are positive, are then followed by interviewer questions. Reliability findings from this recent version are not yet available.

The Structured Interview for *DSM-III* Personality Disorders was devised by Pfohl et al. (15). The questions are grouped topically rather than by individual diagnosis. Whenever a knowledgeable informant is available, the interviewer is encouraged to ask the informant some of the questions; if discrepancies occur between the subject's and the informant's answers, the criterion is scored on the basis of the more valid answer.

The interrater reliability of the *DSM-III* version was reported for the five disorders with calculable kappas (median kappa=0.75, range=0.45–0.90) (16). A subsequent study confirmed good interrater reliability: six disorders diagnosed two or more times had an interpolated median kappa of 0.83 (range=0.65–1.00) (17).

Two instruments have been devised to capture an analogue measure of the certainty of a clinician's judgment about whether a patient meets the criteria for each personality disorder. Hyler et al. (18) devised the Clinical Assessment Form, which was used in a survey study of clinicians contacted by mail. The Clinical Assessment Form includes a 4-point scale for each axis II disorder (0=no traits, 1=mild traits, 2=moderate traits, and 3=fulfills *DSM-III* criteria). Reliability data are unavailable, and the authors cautioned that it is unclear whether these ratings are comparable to true diagnoses.

A second analogue instrument, the Personality Assessment Form, was devised by Shea et al. (19) to assess axis II personality traits in a group of depressed individuals in the Collaborative Study of the Treatment of Depression. The Personality Assessment Form uses a 6-point scale to rate each of the 11 *DSM-III-R* personality disorder diagnoses and the two provisional diagnoses in the appendix. Each scale is preceded by a definition of the important features of the disorder, and each scale point is anchored by a short statement. A diagnosis is considered present if the patient is given a score of 4 (fits the description "to a considerable extent"). The overall reliability of this categorical cutoff score for the instrument yielded a kappa of 0.48. Subsequently, Pilkonis et al. (13) found that the overall interrater reliability kappa was 0.36 on the basis of intake data, 0.44 when follow-up data were available, and 0.49 when knowledgeable informants were interviewed. The 6-month retest stability of kappa was 0.56 for whether any personality disorder was present.

One self-report instrument, the Personality Diagnostic Questionnaire (20), assesses whether the criteria of the *DSM-III* personality disorders are met. The self-report questions of the Personality Diagnostic Questionnaire are arranged by disorder, making it readily scorable. The revised version includes 152 items for the 11 *DSM-III-R* personality disorder types plus self-defeating personality. A yes/no format is used, and the direction of some items is reversed to mitigate problems of response set. The internal consistency of the 11 original Personality Diagnostic Questionnaire scales was reported (median alpha=0.69, range=0.56–0.84) (Kuder-Richardson formula 20) (18).

A second self-report instrument, the Millon Clinical Multiaxial Inventory (21, 22), purports to measure the same construct dimensions represented in the *DSM-III* personality disorder types, although it does not assess the *DSM-III* criteria directly. It consists of 175 true/false questions representing 20 scales. Reich (7) reported moderately high 8-week retest reliabilities (median correlation=0.75, range=0.60–0.89). A revised version is available, with closer approximation to the *DSM-III-R* personality types.

Concern about the validity of single assessment interviews has persuaded some clinicians and researchers to seek alternative ways to make more valid diagnoses. In the absence of a true validity criterion or "gold standard" for diagnoses, Spitzer (23) suggested what has become known as the LEAD standard, referring to making diagnoses based on "longitudinal expert evaluation using all available data." This typically involves using intake diagnostic assessments, past records, data from informants, and, most importantly, observational data from a subsequent inpatient stay and response to treatment. LEAD diagnoses are then assigned on the basis of a review of all the data by a conference of experts, as has been reported in several studies reviewed below (13, 24-26). In one study the 6-month retest stability of kappa was 0.84 for the presence of any personality disorder, although agreement on individual types was not calculated (13).

THE KAPPA STATISTIC AND DIAGNOSTIC AGREEMENT

Interpretation of the level of diagnostic agreement between any two methods is influenced by the base rate or frequency with which each diagnosis is made by each method in the group studied. For instance, if two instruments each diagnose the presence of borderline personality disorder in 40% of a group of subjects, then by chance alone they should agree on the presence of borderline personality disorder in 16% of the cases (i.e., the product of their base rates, $40\% \times 40\% = 16\%$) and agree on the absence of borderline personality disorder in 36% of the cases (i.e., the product of their base rates for nonborderline personality disorder cases, $60\% \times 60\% = 36\%$), for a total chance level of agreement of 52% (i.e., $16\% + 36\%$). The kappa statistic devised by Cohen (27) corrects for chance agreement by taking the base rates into account to calculate what proportion of the maximum possible chance-corrected rate of agreement was obtained. It does this by taking the observed rate of agreement, subtracting the chance rate of agreement, and then dividing that by the maximum possible rate of chance-corrected agreement (i.e., 1 minus the chance rate of agreement). Studies that determine the level of diagnostic agreement between two interviewers or two instruments use the kappa statistic (chance-corrected concordance) rather than simply reporting the percentage of agreement. However, in modest-sized samples, when a diagnosis occurs at a very low base rate, kappa has high variability (28), and so many studies only calculate kappa for diagnoses occurring 5% or more of the time.

Shrout et al. (28), after Fleiss (29), offered the following guidelines in interpreting kappa values: "Values greater than approximately .75 are generally taken to indicate excellent agreement beyond chance, values below approximately .40 are generally taken to represent poor agreement beyond chance, and values in between are generally taken to represent fair to good agreement

beyond chance." A further characteristic of kappa, or weighted kappa, is that in large samples, the weighted kappa is approximately equivalent to the intraclass correlation, interpretable as a proportion of variance (30, 31). Thus, a kappa value of 0.40 suggests that approximately 40% of the variance in the diagnoses made by two instruments is due to true differences in diagnoses among patients, while 60% is due to other things, such as instrument error.

STUDIES COMPARING DIAGNOSTIC METHODS

The following studies compared two or more diagnostic methods. The emphasis of this review is on the concordance of any two methods for making individual personality disorder diagnoses. Because of the special problems in making clinical diagnoses with the use of self-report instruments only, I have included studies that used at least one observer-rated diagnostic method. The findings for individual diagnoses are displayed in table 1.

Perry et al. (32) compared the DIS with a systematic clinical interview on the *DSM-III* diagnosis of antisocial personality in a group of 70 subjects with personality and affective disorders. Antisocial personality was diagnosed by the DIS in 34 cases and by the clinical interview in 20 cases, yielding a kappa of 0.54. The subjects were subsequently reinterviewed two to seven times over a median of 1 year of follow-up. Data on antisocial behavior were systematically obtained by two different interview methods for each follow-up interval. Subjects diagnosed as having antisocial personality by both intake diagnostic methods showed significantly more antisocial behavior than those for whom the diagnosis was either 1) not present according to both methods or 2) not present according to the clinical interview but present according to the DIS. The discrepant cases (group 2) showed no more antisocial behavior than the group that did not have the diagnosis according to both methods.

Hyler et al. (18) compared Personality Diagnostic Questionnaire diagnoses with clinicians' diagnoses. The data on 552 subjects were obtained by a mail survey of psychiatrists. Each participating psychiatrist administered the Personality Diagnostic Questionnaire to two patients and filled out a clinical assessment form, yielding ratings of clinical certainty that the patients met the *DSM-III* criteria for a given diagnosis, although the exact criteria each patient fulfilled were not noted. The diagnostic concordance between the Personality Diagnostic Questionnaire and clinical diagnosis yielded a median kappa of 0.08 (range = -0.16-0.46). When continuous scores were used for both the Personality Diagnostic Questionnaire and the clinical assessment form, the median Pearson's correlation was 0.31 (range = 0.16-0.51).

Zimmerman and Coryell (17) compared diagnoses made by the Structured Interview for *DSM-III* Personality Disorders and the Personality Diagnostic Ques-

TABLE 1. Diagnostic Agreement (kappa) Between Methods of Assessing Personality Disorders in Nine Studies^a

Axis II Personality Disorder	Perry et al. (32) (N=70) Clin. Interview vs. DIS	Hyer et al. (18) (N=552) Clin. Interview vs. PDQ	Zimmer- man et al. (17) (N=697) SIDP vs. PDQ	Hyer et al. (33) (N=87) PDQ-R		Hogg et al. (34) (N=40) SIDP vs. MCMI	O'Boyle et al. (35) (N=20) SCID vs. PDE	Pilkonis et al. (13) (N=40) LEAD		Skodol et al. (26)			Jackson et al. (37) (N=82) SIDP vs. MCMI
				Vs. SCID	Vs. PDE			Vs. PDE	Vs. PAF	Vs. PDE (N=100)	Vs. SCID	Vs. PDE	
Paranoid	—	0.40	0.00	0.27	0.12	—	0.18	—	—	0.29	0.54	0.25	0.19
Schizoid	—	-0.16	0.00	0.43	-0.02	0.18	—	—	—	0.14	—	—	-0.03
Schizotypal	—	0.01	0.27	0.48	0.54	0.34	—	—	—	0.44	0.53	0.34	0.18
Histrionic	—	0.15	0.38	0.24	0.18	0.00	—	—	—	0.58	0.25	0.31	0.12
Narcissistic	—	0.10	0.00	0.34	0.42	0.13	—	—	—	0.44	0.03	0.04	0.25
Antisocial	0.54	0.07	0.14	0.42	0.36	0.15	—	—	—	0.59	—	—	0.06
Borderline	—	0.46	0.30	0.53	0.46	0.00	0.62	—	—	0.53	0.22	0.01	0.53
Avoidant	—	0.10	0.20	0.63	0.53	0.29	—	—	—	0.56	0.23	0.29	0.36
Dependent	—	0.08	0.08	0.57	0.52	0.10	0.23	—	—	0.66	0.60	0.41	0.15
Obsessive- compulsive	—	0.08	0.13	0.30	0.38	—	—	—	—	0.50	0.30	0.06	0.00
Passive-aggressive	—	-0.02	0.00	0.23	0.21	—	—	—	—	0.21	0.03	-0.01	0.38
Self-defeating	—	—	—	0.48	0.31	—	—	—	—	—	—	—	—
Any	—	—	0.32	—	—	—	0.38	0.28	0.21	—	—	—	—

^aDIS=Diagnostic Interview Schedule; PDQ=Personality Diagnostic Questionnaire; SIDP=Structured Interview for DSM-III Personality Disorders; PDQ-R=Personality Diagnostic Questionnaire revised for DSM-III-R criteria; SCID=SCID-II: Structured Clinical Interview for DSM-III-R Personality Disorders; PDE=Personality Disorders Examination; MCMI=Millon Clinical Multiaxial Inventory; LEAD=longitudinal expert evaluation using all available data; PAF=Personality Assessment Form.

tionnaire in a group of 697 relatives of psychiatric patients and healthy control subjects. Experienced interviewers who had completed graduate work in the social sciences were used. Significantly more subjects were given at least one personality disorder diagnosis by the Structured Interview for DSM-III Personality Disorders than by the Personality Diagnostic Questionnaire (17.2% versus 10.3%); however, the Personality Diagnostic Questionnaire gave more multiple diagnoses. Diagnostic agreement between the two instruments was generally poor (median kappa=0.13, range=0.00–0.38), although agreement about the presence of any personality disorder was higher (kappa=0.32). Comparing dimensional scores from both instruments led to somewhat higher levels of agreement (median Pearson's r =0.37, range=0.24–0.55). The largest correlation (r =0.58) was obtained between the total scores of all personality items endorsed on both instruments.

Hyer et al. (33) compared the revised version of the Personality Diagnostic Questionnaire with two structured interviews, the SCID-II and the Personality Disorders Examination, for 87 applicants for inpatient treatment on a personality disorders specialty unit. Interviews were conducted by experienced clinicians on the same day in a balanced order. The revised version of the Personality Diagnostic Questionnaire had relatively low levels of concordance with either structured interview. The median kappa with the SCID-II was 0.43 (range=0.23–0.63), while the median kappa with the Personality Disorders Examination was 0.37 (range=-0.02–0.54). The Personality Diagnostic Questionnaire was found to be highly sensitive to identifying positive diagnoses made by either structured interview (sensitivity range=75%–100%), whereas its specificities

were low (specificity range=24%–89%). The authors suggested that these findings indicate that the Personality Diagnostic Questionnaire might be a useful screening instrument when personality disorders are highly likely to be present, although it is not a substitute for a structured interview. Agreement between the Personality Disorders Examination and the SCID-II is described below from the authors' report on the enlarged sample (26).

Hogg et al. (34) studied 40 hospitalized patients with schizophrenia of recent onset after the patients had recovered from an acute episode. The Structured Interview for DSM-III Personality Disorders and the Millon Clinical Multiaxial Inventory were administered. The Structured Interview for DSM-III Personality Disorders diagnosed personality disorders in 57% of the patients, most commonly yielding antisocial, borderline, and schizotypal types, while the Millon inventory most commonly found dependent, narcissistic, and avoidant types. The level of agreement between the two instruments on eight diagnoses occurring with sufficient frequency was low (interpolated median kappa=0.14, range=0.00–0.34). When dimensional trait ratings were compared, levels of agreement were somewhat higher (median Pearson's r =0.26, range=-0.03–0.60).

O'Boyle and Self (35) interviewed 20 depressed inpatients with the SCID-II (May 1986 version) and the Personality Disorders Examination (May 1985 version) to rate the DSM-III-R criteria. Reliabilities for the diagnoses obtained were acceptable (Personality Disorders Examination, overall kappa=0.63; SCID-II, overall kappa=0.74). Comparing the two instruments, these authors obtained a kappa of 0.38 for the overall presence/absence of any personality disorder. The reliabili-

ties of the three disorders diagnosed five or more times each yielded a median kappa of 0.23, a low of 0.18, and a high of 0.62. The reliabilities did not change appreciably when four subjects who were psychotic at the time of their initial interviews were excluded. The investigators reinterviewed 17 of the patients after they had recovered from their depression to compare effects of the depressed state on the results of the Personality Disorders Examination. The Personality Disorders Examination dimensional scores were lower for all personality disorder types except paranoid when the subjects were in the nondepressed state, and they were significantly lower for borderline and compulsive disorders. The authors concluded that the modest kappas they obtained were of concern.

Pilkonis et al. (13) carried out an elegant study of 40 patients with major depression in which they compared diagnoses obtained from the revised Personality Disorders Examination and the Personality Assessment Form (scored by the same interviewers) and a LEAD consensus method. The diagnosis of mixed personality disorder was included. Because of the small sample size in relation to the number of disorders, they reported only overall levels of diagnostic agreement, rather than agreement for individual disorders. At intake, personality disorders were diagnosed in 80% of the subjects by the Personality Assessment Form, in 70% by LEAD consensus, and in 63% by the Personality Disorders Examination. The overall concordances between methods were 1) for the Personality Disorders Examination and LEAD, kappa=0.28, and 2) for the Personality Assessment Form and LEAD, kappa=0.21. Raising the threshold of the Personality Assessment Form for a positive diagnosis worsened the level of agreement. Personality Disorders Examination data obtained at intake from a significant other as an informant demonstrated higher reliability with the patient's score on the Personality Disorders Examination repeated at 6-month follow-up (kappa=0.50) and with the LEAD consensus data at 6 months (kappa=0.46).

Pilkonis et al. (13) also examined predictive validity, comparing patients diagnosed with and without personality disorders on the amount of improvement at 6 months on the Global Assessment Scale (GAS), the Beck Depression Inventory, and the SCL-90 total score. They hypothesized that patients with personality disorders should show less improvement. The LEAD consensus diagnoses predicted significant differences in improvement on all three measures, while the Personality Disorders Examination demonstrated improvement on the GAS only, and the Personality Assessment Form demonstrated no significant differences.

Skodol et al. (26) compared the SCID-II and the Personality Disorders Examination data on 100 inpatients. Both interviews were independently administered by professionals in balanced order, generally on the same day. Agreement between the two methods was fair (median kappa=0.50, range=0.14–0.66). Comparing dimensional scores from both interviews yielded better agreement (median Pearson's $r=0.77$, range=0.58–0.87).

After at least 6 weeks of inpatient observation, a LEAD diagnosis was made in 34 cases. The SCID-II demonstrated slightly greater agreement with a subsequent LEAD diagnosis (median kappa=0.25, range=0.03–0.60) than did the Personality Disorders Examination (median kappa=0.25, range=–0.01–0.41). The investigators suggested that diagnoses made according to one structured interview should not be considered comparable to those according to another. This conclusion was strengthened in a subsequent report (36) of different patterns of comorbidity between pairs of personality disorder types across the two interviews. In the same sample, out of 55 possible unique pairs, the Personality Disorders Examination found significant co-occurrence in 29 pairs of personality disorders, compared to 12 pairs diagnosed by the SCID-II.

Jackson et al. (37) gave the Millon Clinical Multiaxial Inventory to 82 inpatients prior to discharge and then administered the Structured Interview for DSM-III Personality Disorders the following day. *DSM-III* criteria were used, and the reliability of the Structured Interview for DSM-III Personality Disorders diagnoses was acceptable (median kappa=0.67). The Millon inventory diagnosed more individuals for six of the 11 individual personality disorders. In the comparison of the two instruments, the base rates of the individual disorders varied by a factor between 1.2 and 6.0. The resulting agreement between the two instruments for categorical diagnoses was a median kappa of 0.18 (range=–0.03–0.53). When dimensional scores for each diagnosis were examined, the agreement rose slightly (median Pearson's $r=0.26$, range=0.02–0.63). The authors concluded that for all but the category of borderline personality disorder, the two instruments demonstrated poor concordance, and for some categories they identified completely different individuals.

SUMMARY OF STUDIES COMPARING AXIS II DIAGNOSTIC METHODS

The level of agreement between instruments across the studies in table 1 can be summarized as good news, bad news, and plain news. The good news is revealed by examining the highest kappa value for agreement on individual diagnoses from each study reporting on more than one disorder. This highest estimate yields a median kappa of 0.54 (range=0.34–0.66) and represents fair to moderate levels of agreement. The bad news is obtained by examining the lowest kappa for agreement on individual disorders from the same studies, which yields a median kappa of 0.00 (range=–0.16–0.23), reflecting very poor chance-corrected levels of agreement. Finally, the plain news is summarized by the median value across studies of the median kappa within each study (i.e., the median of the median kappa values): median kappa=0.25 (range=0.08–0.54). This value has the greatest generalization across personality diagnoses across studies. It reflects that on average, the chance-corrected agreement between diagnostic methods is poor.

These values change somewhat if comparisons with self-report measures are treated separately. For comparisons of interview methods only, the median highest estimated kappa=0.61 (interpolated), the median lowest estimate=0.09 (interpolated), and the median of median estimates=0.25. The studies comparing self-report and interviewer methods reported lower values: the median highest estimate=0.50 (interpolated), the median lowest estimate=-0.01 (interpolated), and the median of median estimates=0.16.

As I have indicated, in large samples the kappa is essentially equivalent to the intraclass correlation, interpretable as a proportion of variance (30, 31). An average chance-corrected concordance of 0.25 between instruments (the median values for all methods as well as for interview methods only) suggests that 75% of the variance in personality disorder diagnoses in the average study represents variance not attributable to the patients. This puts considerable constraint on comparing the findings from any one study with those from another. It is not a scientifically acceptable state of affairs.

The overall situation is improved only slightly when dimensional scores for different methods are compared. Of the four studies that did this, the interpolated median Pearson's r values were as follows: highest=0.59, lowest=0.28, and median=0.34. Pearson's r is used to compare scales with different metrics and is not strictly interpretable in the same way as the intraclass correlation or kappa. Nonetheless, the median figure of 0.34 also reflects an overall poor level of agreement.

The finding of poor diagnostic comparability indicates the necessity of testing and improving the measurement validity of methods for diagnosing axis II disorders, a point made by many of the authors I have cited (13, 17, 26, 32). While some authors have suggested that the use of dimensional scores has advantages over categorical diagnoses (38), the evidence I have described suggests that the use of dimensional scores generally did not raise concordance between methods to acceptable levels.

I suggest two different approaches to this problem. The first is to delineate the sources of measurement problems in current instruments in order to improve them. The second is to develop new methods that assess personality disorders in a conceptually different way, with the potential for better measurement validity.

POTENTIAL SOURCES OF MEASUREMENT ERROR IN CURRENT INSTRUMENTS

Early in the development of a field of study, there is a difficulty in disentangling problems due to measurement validity and those involving construct validity (39). Construct validity is demonstrated when findings converge in a coherent way, such as demonstrating validity in the description, etiology, course, and response to treatment of a given personality disorder and demonstrating that these findings diverge from those for other disorders (40, 41). Construct validity is still at

issue for many of the personality disorders and may therefore constrain any test of the measurement validity of a given instrument. Nonetheless, reviews of the *DSM-III-R* personality disorders (42, 43) suggest that there is sufficient evidence to warrant further study of the present types.

Problems with reliability constrain assessment validity. However, most of the observer-rated instruments for assessing axis II disorders have demonstrated fair to high interrater reliability, thereby minimizing this as a major source of discordance. Dimensional ratings, which have even higher reliabilities, demonstrated only slightly higher correlations (17, 34), except in one study (26). Possible sources of the problem are noted below.

The high reliabilities of the instruments suggest that rater variance due to different levels of experience, training, etc. is not a major source of the lack of agreement among instruments. This may be less true for methods that allow for more clinical judgment. However, studies comparing raters with different levels of training or from different sites are largely lacking.

Self-report questionnaires solicit subjective data, whereas observer-rated interviews include observational data, allowing clinical judgment a role in interpreting the subject's responses. The discrepancy between these data sources has been well described (44) and has properly led to caution in interpreting self-report data on diagnoses (17, 18). This is validated by the findings, shown in table 1, that interview methods demonstrated higher levels of concordance with one another than with self-report instruments. For many criteria (e.g., criterion 7 for narcissistic personality disorder: lack of empathy), a subject might be expected to be a poor judge in the self-report, because the phenomenon requires an external judge.

Occasion variance may introduce some disagreement. Theoretically, personality disorder diagnoses reflect *longstanding* characteristics and should have high short-term stability (45). Some studies minimized occasion variance by having the two different assessments on the same day (26, 33), but they still demonstrated problems in diagnostic concordance.

Some instruments may be sensitive to state effects or changes. This may be suggested whenever test-retest stability coefficients obtained within instruments are substantially lower than their reliabilities. In addition, certain instruments, such as the Personality Diagnostic Questionnaire, may be sensitive to state effects due to depression, while other instruments are not (17).

Instruments do not yield the same databases, thereby introducing some information variance (25). They often assess the same criterion with different questions (17), thereby producing somewhat different data. At present it is not clear how representative of its respective criterion each question is. This problem may be amplified for self-report instruments, because each patient's interpretation of a question may be somewhat idiosyncratic.

The yes/no answer format in most instruments may produce a serious problem. First, it is unlikely that in-

dividuals encode their perceptions and attitudes about themselves and their personalities in the same format as that required by the interview. For example, question 79 from the Diagnostic Interview for Personality Disorders (46) inquires of the subject, "[Have you] often noticed that you don't feel things very deeply?" with a follow-up probe, "Have you ever been told that you seemed like a shallow or superficial kind of person?" This question represents a criterion for histrionic personality. It is readily conceivable that anyone who has low self-esteem or, even worse from a conceptual point of view, a compulsive personality, might respond positively. Asking for examples and then following scoring guidelines should mitigate some scoring errors, but to what extent this is true remains unclear. Even when the interviewer requests an example, the yes/no format simply may not develop sufficient information to ascertain whether a positive answer represents a pervasive, long-standing pattern or a sporadic occurrence. Furthermore, there is a danger that some assessments are overly dependent on the subject's self-report when the criterion reflects an objective phenomenon (e.g., constricted affect, restricted emotionality). The reliance on the yes/no question-and-answer format is a very serious issue, given that all of the instruments use it to a large extent.

The LEAD method of diagnosis may minimize some of these sources of variance. However, its reliability has not yet been established, and the use of data from longitudinal observation during an inpatient hospitalization, while attractive, may not represent the patient's real life patterns (25, 26). Pilkonis et al. (13) did find a good 6-month retest stability of their LEAD diagnosis that at least one personality disorder was present ($\kappa=0.84$), although stability of individual disorders would be expectably lower. Unfortunately, the amount of time and personnel required also detracts from the general applicability of the LEAD method, and standardization of procedures remains to be done.

IMPROVING THE CLINICAL INTERVIEW

Structured interviews were originally devised to cut down on the problem of unreliability in the clinical interview. However, it is possible that assessment validity has been neglected in favor of readily obtaining reliability. An examination of how the clinical interview might improve validity while preserving reliability is warranted.

A good clinical assessment of personality begins with taking a history. The clinician asks the patient to tell important stories from across the life span, preserving the life context in which these occurred. Memorable events and important vignettes tell the story of the patient's relationships with family, loved ones, friends, authorities, and co-workers at home, at school, at work, and at leisure. Symptoms and the onset of illness are seen as occurring in a context, and life stress, so important to the patient, is given its due, helping to differentiate the reaction types defined by Adolph Meyer

from the longstanding maladaptive traits that *DSM-III-R* axis II assesses. The database is an aggregate of dramatic or unusual stories balanced by more commonplace vignettes. This results in a more representative sample of behavior and experience than is obtained in response to a format of yes/no questions, even when these are followed by a request for confirmatory examples. Luborsky and colleagues have found that whenever people tell anecdotes about relationships in interviews or psychotherapy sessions, a limited number of patterns of motives, experiences, and interactions can be reliably identified (47). In the clinical interview, the clinician judges that a criterion is met only after reviewing the whole interview and ascertaining that a long-standing pattern is evident in historical context.

There are some challenges that the clinical interview must meet to demonstrate its scientific respectability. Like the structured interviews, the clinical interview must be replicable and yield highly reliable diagnoses. Both of these aims could be accomplished by the development of guides for conducting the interview and the subsequent rating procedures. This would follow a direction that has proven successful in improving the reliability and comparability of psychodynamic formulations (48), a field which shares much treacherous terrain with axis II. Second, a compendium of good case examples demonstrating both common and unusual patterns that reflect axis II criteria would aid in training clinicians to make comparable ratings. This idea is similar to the idea behind the *DSM-III-R Casebook* (49). Third, there is a need for renewed interest in developing training procedures for conducting the clinical interview, as well as standardizing the ascertainment of clinical interviewing competence.

The results of this review suggest that demonstrating the high reliability of a diagnostic method is not enough to answer questions about assessment validity. We now need studies that address validity by comparing the diagnoses made by any two or more methods against some external criterion of validity, such as etiological factors, prediction of course, and treatment response (41). While several studies have begun this work (13, 32, 36), much more evidence is required before we can say that the axis II diagnoses made by any one method are valid. At present, studies using different methods for diagnosing personality disorders on average can be expected to obtain findings that concur at little better than chance levels and reach different conclusions.

CONCLUSIONS

The introduction of structured interviews and self-report questionnaires to assess axis II disorders has resulted in improved diagnostic reliability within each method. However, comparisons of any two instruments used with the same subjects reveal more diagnostic disagreement than agreement on average. Using continuous or dimensional scoring improves the situation only marginally. This suggests that studies using differ-

ent diagnostic instruments can be compared only with great caution. Whether instruments for which no comparison studies are available (46, 50) will demonstrate better diagnostic concordance remains unknown, but their interview formats are by and large similar to those I have reported. More work on improving the validity of axis II assessments is needed.

There may be a variety of reasons for problems with current approaches. Some, such as variance due to different raters, interview occasion, and state changes, are well-known. Other reasons may be more specific to the problem of assessing personality features, such as establishing that a specific pattern is pervasive and present over time. Using a guided clinical interview offers one potential solution to this problem. Further study is required to determine the assessment validity of current methods for diagnosing personality disorders.

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Measuring the Determinants of Work Values for Psychiatrists' Services in the Resource-Based Relative Value Scale Study

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Objective: As part of the Harvard resource-based relative value scale study, the authors investigated how well the codes in the Physician's Current Procedural Terminology, 4th edition, or CPT-4, match psychiatric services to the work involved in evaluating and managing patients and how patient care characteristics affect different levels of psychiatric work. **Method:** A random sample of over 200 psychiatrists and subspecialists was asked to use 68 typical clinical examples or vignettes to evaluate services described by CPT codes. Data were analyzed by multivariate statistical methods. **Results:** The survey showed that the existing coding system does not adequately describe the work that psychiatrists do. Within a single code (e.g., 90844, individual medical psychotherapy), there was wide (more than twofold) variation in the estimates, from multiple measurements based on different vignettes, of the amount of work represented. Estimates of work values varied significantly according to treatment setting and patient characteristics: psychiatric services in the hospital showed an average work value 25% greater than that for office services; treating new patients involved 18% more effort than treating established patients; and treating patients described as at risk of harming self or others increased the psychiatrists' work effort by 36%. **Conclusions:** Revisions in coding evaluation and management services in the new Medicare fee schedule for psychiatric services should be further refined and then implemented. These revisions would bring the coding system into line with psychiatric practice, making it a better way of accounting for the relative work involved in treating patients of varying difficulty.

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In announcing the final Medicare fee schedule required in 1989 by federal legislation, which mandated physician payment reform (Public Law 101-239), Gail Wilensky, the administrator of the Health Care Financing Administration, called the new Medicare fee schedule "the most significant change in the way Medicare pays doctors . . . since the program began. More importantly, the changes create more equity and consistency in payments to physicians" (Boston, Nov. 22, 1991). The legislation was designed to encourage primary care evaluation and management services, rather than invasive specialty services, by reducing the differences in payments between categories. Under the new Medicare fee schedule, payments will be set nationally, primarily on the basis of the "resource-based relative value scale." The

Medicare fee schedule takes into account physicians' work, overhead, and malpractice costs associated with providing a service; the final Medicare fee schedule is adjusted for geographic variation in practice costs, professional liability insurance, and cost of living (1).

In order to create the Medicare fee schedule, the Health Care Financing Administration worked with a group of researchers at the Harvard School of Public Health under the direction of economist William Hsiao. Over 30 different specialties were studied by the team with the help of numerous specialty consultants. As part of the Harvard resource-based relative value scale study team, and with support from the National Institute of Mental Health, we were responsible for development of the resource-based relative value scale for psychiatry. As described in this article, we obtained relative work values for the full range of psychiatrists' services. In addition, we carried out statistical analyses intended to explain the factors that determine variations in the value of the work done by psychiatrists. We believe these results have implications for potential reform of service codes, which are used in most third-party billing for psychiatrists' services, and for understanding the relation between the coding system and reimbursement for evaluation and management services. Since Medicare intends to reexamine and, where necessary, modify the Medicare fee schedule periodically, our findings may contribute to future coding reforms.

Implementation of the Medicare fee schedule has required changes in the *Physician's Current Procedural Terminology, 4th edition (CPT-4)* codes which physicians use to report evaluation and management services that they have performed. The evaluation and management services are defined to include making diagnoses, counseling and educating patients, developing strategies of care, and following up on treatment. These evaluation and management services are especially relevant for psychiatric practice. In order to assign accurate relative values (defined below) to these services and to ensure equitable payment under the fee schedule, codes must be interpreted and used uniformly by the physicians in a specialty and in all regions of the country. This is not the case with *CPT-4* codes (2).

The Medicare fee schedule requires that *CPT-4* codes represent similar resource costs to all who use them. We wished to answer the question, How much variation is permissible before resource costs are to be considered dissimilar? Deciding how wide a range of work values may fall within the scope of a single code that is used for billing is an important issue which must be addressed in crafting a coding system. Wide ranges may result from ambiguity in the definition of the code, differences in physician practice styles, or heterogeneity of types of service provided. When the range is large, physicians who regularly provide services at the low end of the range of work values will be relatively overcompensated for that code, while those whose services are regularly at the high end will be undercompensated. Too wide a range of work values in the framework of a fee schedule provides an incentive to provide services at the low end of the range.

In previous research, the Hsiao group found that the range of variation within a code for most medical evaluation and management services lies within 30% of the mean (3). On the basis of these findings for evaluation and management services studied in other specialties, we propose that visit codes in which physician work varies by more than a twofold difference not be used for payment purposes and that the service be coded into better-defined categories to specify the content of the work for each code.

In this article we analyze two aspects of variation in the work values of psychiatrists that are important for designing a better payment system for psychiatry. First, we identify services for which there is at least a twofold variation within a code. Second, we examine characteristics of patient care that may influence the level of work. Importantly, these characteristics are not currently incorporated into the *CPT-4* coding system for specialty-specific psychiatric services.

We formed a panel of psychiatrists, selected by a process previously described (4), to constitute a Technical Consulting Group for psychiatry. Physicians' work for each service is measured to take into account the time required to provide the service (in minutes) and three factors that determine the intensity of work for the time spent: 1) the mental effort, knowledge, and judgment required, 2) the technical skill and physical effort expended, and 3) the level of stress, due to risk to the patient or others, including the physician. In our investigation, intensity was measured operationally as the work per unit time required to perform a particular service (5).

We elicited suggestions from the Technical Consulting Group for factors that were thought to influence the intensity of psychiatrists' work. It was suggested that for a particular service (e.g., psychotherapy), the range of intensity would vary, depending on characteristics of the patient, the nature of the treatments provided, the setting of care, and other factors specific to the services provided. For psychiatry, the factors that were hypothesized to be associated with different levels of intensity included site of treatment (office and hospital), age group of the patient, whether the patient is new or established, management of psychotropic medications, number of people seen in a session, and the degree of risk of harm by the patient to himself/herself or others (dangerousness).

METHOD

The general method for construction of the resource-based relative value scale and for the estimation of work values is described in detail elsewhere (6). In collaboration with APA, we used definitions of services based on *CPT-4* to develop a list of the 68 most frequently performed services. In order to measure the range of work values of commonly used *CPT-4* codes, we composed for each of these codes clinical vignettes of varying complexity and severity of symptoms that

require varying durations of treatment. We included most of the available CPT-4 billing codes used for psychiatric services and added several services for which there were no specific CPT-4 codes, such as play therapy for a young child. We then obtained for each vignette, through a national survey, ratings of the intraservice and total work involved. The "total work" includes time actually spent with the patient during an encounter in the office (intraservice) plus time spent in preparation before the visit and on follow-up activities related to the encounter (6).

To illustrate, several vignettes representing varying treatment complexity were constructed for psychiatric services. One vignette was selected by the psychiatrists of the Technical Consulting Group as typical of a psychotherapy visit, and others were devised to be more or less difficult. The standard vignette chosen for comparison was the following: "50 minutes of psychotherapy in the office, fourth session, for a married 25-year-old male, originally referred by an internist, suffering from the recent onset of panic attacks. The panic attacks have not interfered with his employment, and he is responding positively to medication and psychotherapy." For purposes of comparison, this service was given a value of 100. An example of a vignette of a service of relatively greater difficulty is "one session of psychotherapy in the office, for a 45-year-old male with a five-year history of a bipolar mood disorder, who is on lithium carbonate and is seen every other week for issues related to conflict in his marriage and at work, and who reveals a plan to kill himself during the session. After assessment you take steps to begin involuntary admission to the hospital." The study sought to quantify, on the basis of estimates by practicing psychiatrists, the magnitude of the difference in work values between these two services, based on the definition of work mentioned above. Clearly, the second service requires more time, mental effort, and judgment and entails greater risks during and after the visit. It not only requires more time but requires a higher intensity of work. Respondents assigned a numerical rating of 235 to this vignette, indicating that it is more than twice as difficult as the standard.

A random sample of psychiatrists was drawn from the American Medical Association (AMA) 1988 Physicians' Masterfile. The sample was stratified geographically by 10 census regions and by specialty-specific distributions within each region. Board-certified psychiatrists represented approximately 80% of the sample. We excluded psychiatrists who worked fewer than 20 hours a week in patient care or who were in residency training. After mailing questionnaires to our sample, we obtained their responses shortly thereafter in telephone interviews conducted by a professional survey organization. Respondents rated services with the method of magnitude estimation, comparing the work of all psychiatric services to the reference standard service vignette described earlier (7).

We further divided the sample into three parts, with an oversample of psychoanalysts and child psychiatrists

in the second and third subsamples, respectively. Survey questions were correspondingly matched to the respondents, so that certain basic core services were presented to all respondents, but services for children were presented primarily to the child psychiatrists. We questioned whether there were systematic subspecialty differences in work values within psychiatry and tested for this possibility with an analysis of variance (ANOVA). Each psychiatrist was classified according to primary subspecialty: child psychiatry, psychoanalysis, or general psychiatry. The Technical Consulting Group consultants felt that further division of the sample into additional subspecialties was unlikely to be necessary. An ANOVA was performed on each group (i.e., child psychiatrists, psychoanalysts, and general psychiatrists) and on the entire sample for a common set of core services, with physician and service as independent variables. When we compared the sums of squares for the interaction terms, we found little variation (less than 2%), suggesting little difference in estimates of total work across the three groups.

We used multiple regression techniques to analyze the determinants of work value for the total work of the service (preservice, intraservice, and postservice work) as well as for intraservice work alone; however, only results from using total service as the dependent variable are reported here. A set of independent variables measuring possible predictor variables of work value was then created. We analyzed the residuals of our model for randomness, normality, constancy of error variance, and appropriateness of the regression function. We also examined the independent variables to ensure that there was no significant multicollinearity.

RESULTS

Of an initial sample of 300 psychiatrists drawn from the AMA 1988 Physicians' Masterfile, 209 completed the survey—a 71% response rate. We found that 25% (N=52) of our sample were child psychiatrists, 17% (N=36) were psychoanalysts, and the remaining 58% (N=121) were general psychiatrists or other subspecialists.

Eighty-three percent of the sample was male, and the average age was 51.5 years. Eighty-two percent of the respondents were board certified, and the average net income was \$118,000 per year. We asked psychiatrists to describe their most recent week's work, separating their practice activities into several categories of work (e.g., total hours worked, hours in the office). The typical psychiatrist reported spending 51 hours per week at work, excluding time spent on-call (an additional 9 hours per week). The characteristics of the respondents were similar to the ones described in *The Nation's Psychiatrists* (8), but the group differed slightly from the general population of psychiatrists in being slightly older, spending a few more hours per week seeing patients, and having a higher proportion of board-certified physicians.

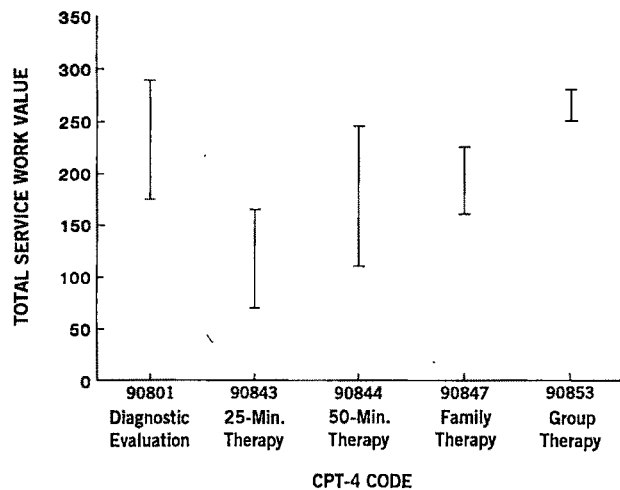
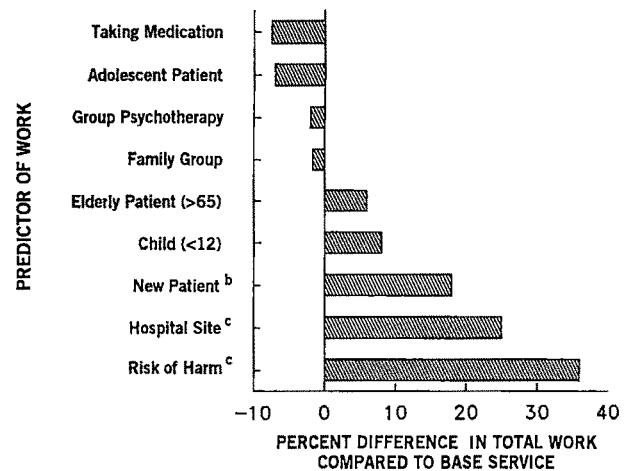
FIGURE 1. Range of Variation of Total-Service Work Values Within Selected CPT-4 Codes for Psychiatry

Figure 1 presents the range of observed total work values for selected CPT-4 codes for psychiatry. All five codes exhibited some variation in the mean work values associated with a vignette or description; CPT-4 codes 90843, 90844, and 90801 for psychotherapy and diagnostic/evaluation services varied twofold or more from the lowest to the highest value. When compared to the smaller average variations in work values described in other medical services, such large variations in the work values within the CPT-4 code suggest that the code may be too general and covers more than one distinct service. We decided to look at these psychiatric services and to analyze their determinants of work values by calculating total-service work values for the selected psychiatric services described in figure 1. For the most common services, such as individual psychotherapy or group and family therapy, the total work value for the code was a weighted average for several vignettes. Group psychotherapy was calculated per patient. These relative values were derived for use in the Medicare fee schedule; however, in our subsequent analysis reported below, we sought to explain underlying reasons for the variation in total work value across different examples of a service within a single code.

Figure 2 shows how our hypothesized characteristics affect total work values for the services described by the CPT-4 codes shown in figure 1. The base service is set arbitrarily at 100 work units (e.g., a typical office visit for an established patient, an adult under age 65, who is taking no psychotropic medications and is not at high risk of harm).

If the session is for a new patient, defined as the first three visits, the total work value is 18% greater than for an established patient. If there is evidence for potential harm to the patient or someone else, total work value increases 36% on average. When the service is provided in the hospital, the work value increases by 25%. When effects are combined, the work value of a visit can vary more than twofold. For example, the work of an initial

FIGURE 2. Percentage Change in Total-Service Work Values for Selected Psychiatric Services in All Settings^a

^aThe base service is an individual encounter in the office with an established patient who is not taking medication and is not at risk of causing harm to self or others. Percentage differences in total work values are compared to base service.

^bSignificant difference at the 0.05 level.

^cSignificant difference at the 0.01 level.

session of psychotherapy in a hospital with a patient who is potentially dangerous to himself has a work value more than twice that of the base service, although both services take the same amount of time.

In addition to the variables shown here, we included time as a determinant of work value for psychiatric services. Our results show that for an increase of 1% in the time of a visit, total work increases by 0.8%. Thus, when all other characteristics of the regression are held constant, the results show that work value increases relative to time, but at less than a 1:1 ratio. If the value of a 50-minute visit is 100, then a 25-minute visit will have a relative work value of 60. As was found to be the case in other medical specialties, time appears to be the single most important determinant of work value for psychiatric services.

DISCUSSION

The resource-based relative value scale approach to payment will make an important change in payment for all physicians, but especially for those providing evaluation and management services. Psychiatry stands out as one specialty in which time spent with patients plays a very important role. The most commonly provided office-based service is psychotherapy, in which time spent with patients is a crucial aspect of treatment (9). Our results indicate the importance of time in assessing psychiatrists' work, but in addition we have shown that, holding time constant, services billed using the same CPT code category may vary widely in intensity or difficulty.

We found that three variables reached statistical sig-

nificance as factors influencing the intensity of work: new patients, hospital care, and risk of harm. New psychiatric patients require more effort than established ones, as is the case in medicine generally. The evaluation of such patients requires careful and thorough interviewing, formulation of a differential diagnosis, and often the gathering of collateral information and data. It is also reasonable to assume that on average, patients treated in the hospital are more acutely ill and require greater diagnostic efforts and more complex treatment interventions than those seen in the office. This fact is recognized by the idea of payment of the physician for "floor time" in the hospital, involving coordination of care, review of records, and interaction with staff members on a treatment team. Patients who are likely to be at risk of harming themselves or others are more difficult to treat than nonthreatening patients. Risk of harm on the part of the patient increases the importance to society of the physician's judgment and often increases the potential medical malpractice liability for the physician and the hospital.

The finding concerning dangerousness of the patient deserves further clarification. Dangerousness in this study included a variety of aspects of potential risk of harm to self or others, including ideas or plans for self-destructive behavior. This is necessarily a limited definition of dangerousness, somewhat akin to the standards used by many state governments to evaluate individuals for civil commitment. Obviously, many patients have self-destructive symptoms but are not candidates for hospitalization; making this clinical judgment is a frequent burden of treatment for psychiatrists.

The finding of the importance of dangerousness in the weighting of estimates of work values raises perplexing policy issues in designing a physician payment system, such as how to verify the clinician's judgment about the degree of dangerousness if the diagnosis would result in higher charges for the treatment. Another problem is how to design a billing and reporting system that would not violate patient confidentiality. This problem of confidentiality arises in psychiatry because of the stigma associated with a diagnosis of schizophrenia, for example, and in other specialties in designing payment for treating medical patients with AIDS or addictions, for example. We are faced with the dilemma of how to take into account the need to compensate physicians for the important clinical work that they do, while at the same time protecting patients' rights to privacy and recognizing limitations of providers' judgment.

In addition to the variables we found to be statistically significant, there were others for which we found some variation that did not reach statistical significance. These variables describe factors that we hypothesize may have an influence on the intensity of work but which require further investigation. For example, psychiatrists rated services involving the treatment of young children as requiring more work than services for adults. Perhaps this is related to problems in communication requiring the interpretation of non-

verbal behavior and fantasy play, or perhaps it is related to the need to spend additional time in family interactions. Other variables, such as the influence of medications, are difficult to interpret and deserve further study. Certain specific categories of services also required considerably more work, not just more time, than did regular psychiatric office visits. Forensic consultation was one of these; however, there is currently no CPT-4 code for this service.

What are some of the implications of our analysis for coding psychiatric services? The wide range of variation in work values for the psychotherapy code (90844), which specifies 45- to 50-minute sessions, raises the question of whether it should be divided into two or three different levels of care. The finding that services provided in the hospital require more work on average than do comparable services in the office suggests the need to examine whether there should be a different code assigned according to the setting in which the services are provided. Proposals for coding according to setting for psychiatric services provided to partially hospitalized patients and those in residential care settings are now being developed; new codes for other psychiatric interventions in other settings, such as the emergency room, may also be desirable. The finding of greatly increased work associated with potential dangerousness deserves further investigation and discussion of coding options.

CONCLUSIONS

This study demonstrates that the classification and coding system on which the resource-based relative value scale is based—CPT-4—inadequately captures the breadth and depth of practice in psychiatry. We found a range of variation within CPT-4 codes for commonly provided services, such as the psychotherapies, that extends beyond the bounds that might be considered reasonable or desirable for a uniformly applied reimbursement system. Our findings suggest the need for further refinement of codes for psychiatry. Our findings may be useful because Medicare intends to make needed adjustments and revisions annually for the Medicare fee schedule.

In this study, we demonstrated that there are identifiable clinical and situational aspects of psychiatrists' work that show a statistically significant amount of variation in both the intraservice work and the total work of psychiatric services: new patients, work in the hospital, and potential dangerousness of patients. These findings raise important questions about the current structural basis used by Medicare for the implementation of a fee schedule for psychiatric evaluation and management services. Two of the determinants of work value identified in our analysis could be incorporated into the new Medicare fee schedule and would lead to a system in which coding and payment would be more closely related to physicians' work. The status of the patient (new versus established) and the site of

care (office versus hospital) can be reliably verified and operationalized. Dangerousness as a patient coding characteristic is, as we noted, more problematic. As implementation and refinement of the Medicare fee schedule for psychiatry proceed, we believe that further efforts to address the issues identified in this study may lead to a fairer payment system.

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Assessment of Lineality in Bipolar I Linkage Studies

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Objective: To assess lineality in families of bipolar I probands, the authors used direct interviews of family members to reclassify families initially categorized as unilineal by family history. **Method:** The families of 1,800 treated bipolar I probands were screened by the family history method with multiple informant. If the proband had one or more affected sibs and one apparently unaffected parent, the parents (and then other available first- and second-degree relatives) were directly interviewed by psychiatrists. **Results:** Of the 1,800 families screened, 56 were apparently suitable unilineal families with multiple affected members; 46 families were interviewed directly. After interviews with the parents, 12 families (26.1%) were found to be bilineal. Direct interviews of all available relatives in the 34 remaining families revealed that only 22 (47.8% of the 46 interviewed families) were unilineal or probably unilineal and 12 were probably bilineal. The probably bilineal families had a significantly higher proportion of siblings with unipolar disorder. In addition, the affected sibs from the probably bilineal families tended to have earlier onsets but had significantly fewer symptoms in the most severe depressive episode. **Conclusions:** Fewer than 50% of bipolar I families appearing unilineal according to family history were found to be unilineal by direct interviews. The phenotypic differences between the affected sib from the probably bilineal families and those from the unilineal and probably unilineal families suggest differences in genetic mechanisms. These findings highlight the need to systematically assess lineality in all families considered for bipolar I linkage studies.

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The importance of genetic heterogeneity as a potential problem in resolving the genetics of bipolar I affective disorder has been widely discussed (1-5). The related issue of bilineality (the existence in both parental lines of the same illness that affects the proband) has received less attention (5, 7). The phenomenon of mating by two individuals with major affective disorders is common and may represent assortative mating (8-11), although other explanations are plausible. Since bilineal families may introduce into the family's gene pool more than one gene that contributes to the bipolar I phenotype, they present a substantial problem for ge-

netic linkage analyses, which can detect efficiently only one disease gene per family. Therefore, carefully selected unilineal families are required to test the hypothesis that some forms of bipolar illness have mendelian (monogenic) inheritance. The mendelian hypothesis will not have been tested rigorously until a sufficient number of unilineal bipolar I families have been completely genotyped, by using genetic markers spanning the entire genome, and analyzed.

Since the limits of the phenotypes associated with the bipolar genotype(s) are not clear, there is some uncertainty about which families are unilineal and which are bilineal. Most studies (12-14) suggest that the phenotypes considered to be affected should include bipolar disorders, schizoaffective disorder—manic, and recurrent unipolar disorders, but it is possible that other clinical conditions, when seen in a family ascertained through a bipolar proband, also may be manifestations of the bipolar genotype (15). The Research Diagnostic Criteria (RDC) (16) diagnoses of single episodes of major depressive disorder, hypomanic disorder, intermittent depressive disorder, agoraphobia, panic disorder, and obsessive-compulsive disorder and DSM-III-R diagnoses of pathological gambling, anorexia nervosa,

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and bulimia nervosa have all been associated with affective disorder in one or more family studies (15, 17, 18). If these uncertain phenotypes are ignored in the supposedly unaffected parent of a bipolar proband but are, in fact, genetically related, then bilineality would not be detected. If, on the other hand, these phenotypes are genetically unrelated to bipolar disorder, then such families would be unilineal.

There are widely differing views as to what constitutes bilineality and how to handle it in linkage analyses. Merikangas et al. (6) believe that a family in which both parental lines have any of the conditions which have been associated with affective disorder may be bilineal and should not be accepted for genetic linkage studies of bipolar disorder. Bilineality may have contributed to the loss of evidence favoring linkage to chromosome 11p loci in the reevaluation of the Old Order Amish study. The pedigree, as described in published reports, contains three affected but apparently unrelated individuals among the progenitors (19). In a negative study using X-chromosome markers, Berrettini et al. (14) excluded branches of families clearly affected by bilineality but left unexamined one-third of the fathers assumed to be unaffected but who had affected offspring. If any of these fathers were affected, they may have passed on to their offspring an autosomal form of the disease.

Since currently it is not possible to know which families are truly unilineal, we have examined directly both parental lines of probands for evidence of affected or uncertain phenotypes. We report here clinical data from 34 families that, after direct interviews of both parents, siblings of the proband, and all other first-degree relatives, were classified as unilineal, probably unilineal, or probably bilineal.

METHOD

Initially we selected families that each contained a treated bipolar I proband with two or more siblings who were affected with bipolar I disorder, schizoaffective disorder—manic, bipolar II disorder with recurrent major depressions, or recurrent unipolar disorder. Currently we are ascertaining families through treated bipolar I probands with one or more affected sibs. We require that the assumed unaffected parent be alive and available for examination.

To find suitable families, we screen the psychiatric inpatient units, day treatment center, and outpatient clinics at a university hospital and an urban medical center in Baltimore. Our collaborators in Iowa screen the psychiatric inpatient and outpatient units at a university hospital.

When we find a prospective study family, we obtain informed consent, take a thorough family history of both parental lines from multiple informants (20, 21), and tentatively assign the family to one of four categories: 1) unilineal, 2) probably unilineal, 3) probably bilineal, and 4) bilineal. These are defined as follows:

1. *Unilineal*—the required unaffected parental line (parent, sibs of the parent, and grandparents) has no phenotypes classified as uncertain or affected.

2. *Probably unilineal*—the required unaffected parental line has no affected phenotypes but has some uncertain phenotypes.

3. *Probably bilineal*—the required unaffected parent has a parent or sibling with an affected phenotype.

4. *Bilineal*—both parents are affected.

Families that appear unilineal or probably unilineal are studied further by means of direct interviews. All available relatives are interviewed by one of two psychiatrists (S.G.S. or J.R.D.) with the Schedule for Affective Disorders and Schizophrenia—Lifetime Version (SADS-L) (22), to which we have added supplemental questions on medical conditions, pathological gambling, eating disorders, and treatment response. A blood sample is obtained to establish a lymphoblastoid line. If, by SADS-L interview, a key member of the “unaffected” parental line is diagnosed as having an affected phenotype, the family is designated as bilineal or probably bilineal and is not used for linkage analysis.

Diagnoses are made by using the RDC (16). A best-estimate diagnosis is made on the basis of the SADS-L data and information from psychiatric records, the individual's treating psychiatrist(s), and first-degree relatives. To avoid false positive diagnoses in siblings, we use a narrow definition of the affected phenotype. To detect bilineality (introduced by grandparents and parental sibs, as well as parents) we also use a narrow definition of the unaffected phenotype. An individual with an associated condition who cannot be confidently categorized as either unaffected or affected is designated as having an uncertain phenotype. The category of uncertain phenotype includes individuals with 1) threshold cases of affective disorder, such as hypomania, intermittent depression in the absence of recurrent major depressive episodes, or a single episode of major depression; 2) nonaffective conditions, such as panic disorder, obsessive-compulsive disorder, and anorexia nervosa; and 3) probable phenocopies, i.e., affective disorders secondary to physical illnesses (e.g., stroke and hypothyroidism), trauma, or medications.

The statistical analyses used were chi-square analysis of discontinuous variables, analysis of variance with post hoc analysis for continuous variables, and analysis of the age-adjusted residuals to take into account the differences in age at interview across groups.

RESULTS

To date, we have screened more than 1,800 bipolar I pedigrees and have systematically recorded the reasons for rejection for the last 1,488 pedigrees screened. The reasons for rejecting families on the basis of family history were, in descending order of frequency, insufficient number of living relatives (29.2%), obvious bilineality (20.6%), refusal to participate (16.2%), insufficient number of affected relatives (12.3%), unsuitable pro-

TABLE 1. Age and Sex of 34 Bipolar I Probands and Their Parents and Siblings in Families Classified as Unilineal by Family History and Reclassified by Direct Interviews

Lineality According to Direct Interviews	Number of Families	Probands					Parents					Siblings				
		N	Sex		Age (years)		N	Sex		Age (years) ^a		N	Sex		Age (years) ^b	
			M	F	Mean	SD		M	F	Mean	SD		M	F	Mean	SD
Unilineal	12	12	9	3	32.9	9.9	19	13	10	66.9	7.8	33	15	18	41.7	11.5
Probably unilineal	10	10	4	6	36.7	7.3	17	8	9	60.1	5.2	35	18	17	33.3	13.0
Probably bilineal	12	12	7	5	31.6	13.2	22	11	11	57.9	5.8	28	15	13	28.3	7.0

^aParents in unilineal families significantly older than parents in other groups ($F=11.94$, $df=2, 55$, $p<0.0003$). Significant differences between parents in unilineal families and those in probably unilineal ($p<0.01$) and probably bilineal ($p<0.001$) families (Scheffé test).

^bSiblings in unilineal families significantly older than siblings in other groups ($F=1.68$, $df=2, 93$, $p<0.0002$). Significant differences between siblings in unilineal families and those in probably unilineal ($p<0.02$) and probably bilineal ($p<0.001$) families (Scheffé test).

TABLE 2. Phenotypes in 96 Siblings of 34 Bipolar I Probands in Families Classified as Unilineal by Family History and Reclassified by Direct Interviews

Lineality According to Direct Interviews	Number of Siblings	Siblings' Phenotypes									
		Affected (N=62)						Uncertain (N=18)		Unaffected (N=16)	
		Bipolar I		Bipolar II		Unipolar ^a		N	%	N	%
		N	%	N	%	N	%				
Unilineal	33	9	27	9	27	2	6	6	18	7	21
Probably unilineal	35	7	20	13	37	4	11	6	17	5	14
Probably bilineal	28	4	14	6	21	8	29	6	21	4	14

^aSignificant difference between siblings in unilineal families and those in probably bilineal families ($\chi^2=5.60$, $df=1$, $p<0.02$).

band (12.1%), and unavailability of key relatives (6.3%). The most striking finding was that many families that initially appeared suitable later had to be excluded for bilineality. Of the families meeting the family structure requirement of at least two affected sibs (including the proband), 50% had to be excluded because of bilineality after more family history was obtained and/or direct interviews were done.

On the basis of family history, 56 families were accepted, and the parents in 46 of these families were interviewed. Twelve families were dropped after this stage because of bilineality. Most of the sibs and other available family members in the 34 remaining families were interviewed. Ten of the 68 parents were not interviewed (eight were deceased, and two refused), and 26 of the 122 siblings were not interviewed, mostly for geographical reasons; none of the un interviewed family members were included in the data set. After direct interviews with all available family members, we reclassified 12 of these 34 families as unilineal, 10 as probably unilineal, and 12 as probably bilineal. Table 1 shows the age and sex of the probands, parents, and siblings in these 34 families. There were no significant group differences in the sex ratio for either the probands or the siblings when affected and unaffected sibs were considered together. There were significantly more male unaffected sibs than female unaffected sibs in the probably bilineal group ($\chi^2=4.37$, $df=1$, $p<0.05$). While the average ages at interview were similar in the three proband groups, there were significant differences in age among the parents and siblings: the parents and sibs were oldest in the unilineal families and youngest in the probably bilineal ones (table 1).

Probands

The bipolar I probands from the 12 unilineal, 10 probably unilineal, and 12 probably bilineal families were compared in terms of characteristics of depression and mania. There were no significant differences in the number of symptoms, number of episodes, age at onset, longest duration of an episode, or number of hospitalizations for either mania or depression between the bipolar I probands from the unilineal families and those from the probably unilineal and probably bilineal families.

Siblings

Because all the families were required to have at least two affected siblings, the prevalence of affective disorder was high in all three groups (table 2). The sibs in the probably bilineal families had a significantly higher rate of unipolar disorder than did the sibs in the unilineal families, 29% versus 6% (table 2). There was a higher proportion of bipolar I sibs in the unilineal families than in the probably bilineal families, but this difference did not reach significance.

As shown in table 3, the affected sibs in the unilineal families had significantly more symptoms in the most severe depressive episode than did those from the probably bilineal families. The affected sibs from the three types of families were also compared with respect to age at first outpatient treatment and number of hospitalizations. Because age at interview was significantly different across the three groups, this variable was taken into account by using age-adjusted residuals. The sibs from

the unilineal families tended to be oldest at first outpatient treatment, and those from the probably bilineal families were the youngest (table 3). The number of hospitalizations was not significantly different across the three groups.

DISCUSSION

The purpose of this paper is to describe our experience with a two-stage method for assessing lineality in bipolar I families ascertained for a genetic linkage study. We found that fewer than one-half of the families who appeared to be unilineal according to family history were unilineal according to direct interviews. There were phenotypic differences between the affected sibs from the unilineal and the probably bilineal families. The probably bilineal families had a significantly higher proportion of sibs with unipolar disorder. In addition, the sibs from the probably bilineal families tended to have an earlier onset but had significantly fewer symptoms in the most severe depressive episode.

High Prevalence of Bilineal Families

Our initial plan, based on the requirements of our linkage analysis design, was to ascertain unilineal families with three or more affected sibs. Clearly unilineal families with this structure have proven difficult to find. Even after we changed our family structure requirement to include families with only two or more affected sibs (including the proband), almost one-half of the families appeared to be bilineal. This experience is consistent with the results of the study of affected siblings of probands with bipolar mood disorder by Pritz and Mitterauer (23), who found that as the number of affected sibs per family increased, so did the probability that the family was bilineal. Their information on affected family members was based largely on hospital records, sometimes going back six generations. Sixty-eight percent of their families with three affected sibs were bilineal, compared to 46% of their families with two affected sibs.

Some of the bilineality may be accounted for by assortative mating, the tendency for mated pairs to be more similar for some phenotypic trait than would be expected if they were chosen at random. Merikangas and Spiker (11) studied the spouses of 56 affectively ill inpatients and found that 54% had lifetime histories of some psychiatric illness and 43% had lifetime histories of affective disorder. Eighty-five percent of their bipolar inpatients had spouses with histories of some psychiatric disorder, compared to 45% of the unipolar inpatients. However, this does not clarify the genetic importance of bilineality in general or assortative mating in particular in the transmission of bipolar disorder. Assortative mating could complicate linkage studies in a mendelian dominant (but genetically heterogeneous) disease by producing affected offspring who have different genotypes. On the other hand, assortative mating

TABLE 3. Clinical Features of 62 Affected Siblings of 34 Bipolar I Probands in Families Classified as Unilineal by Family History and Reclassified by Direct Interviews

Lineality According to Direct Interviews	Siblings' Characteristics					
	Age at First Outpatient Treatment (years) ^a		Number of Admissions		Number of Depressive Symptoms in Most Severe Episode ^b	
	Mean	SD	Mean	SD	Mean	SD
Unilineal	20.5	13.1	2.2	3.2	7.5	0.7
Probably unilineal	17.8	11.2	1.8	4.1	6.9	1.0
Probably bilineal	13.8	9.2	0.9	1.8	6.5	1.5

^aNearly significant difference between siblings in unilineal families and those in probably bilineal families ($F=2.34$, $df=2, 58$, $p=0.06$).

^bSignificant difference between siblings in unilineal families and those in probably bilineal families ($F=3.85$, $df=2, 53$, $p=0.02$).

could contribute to the high prevalence of a polygenic disorder and produce mendelianlike segregation ratios in nuclear families.

Possible Explanations for Clinical Differences Between Unilineal and Probably Bilineal Families

Comparison of clinical data from the unilineal and probably bilineal families suggests that the unilineal families may have a mendelian form of bipolar disorder. First, 90.0% of the affected siblings had bipolar I or II disorder (table 2). This contrasts with the probably bilineal families, in which a significantly higher proportion of the siblings had unipolar disorder. Second, the affected sibs from the unilineal families had significantly more symptoms in their most severe episodes of depression than did those from the probably bilineal families. On the other hand, those from the probably bilineal families had a younger age at onset.

In the probably bilineal families, the offspring may be getting different genes (possibly major and minor) for affective disorder from both parents, and thus one would expect to see more of a spectrum of affective disorders in those families. It may be that if both parents are carrying minor genes for affective disorder, their offspring are more likely to develop unipolar than bipolar disorder.

The greater number of symptoms in the most severe depressive episode in sibs from the unilineal families than in sibs from the probably bilineal families may indicate that where bipolar disorder breeds true, it is more severe.

We have no explanation for the finding that the siblings from the probably bilineal families were significantly younger than those from the unilineal families at the time of the study; it may be a spurious finding. We are presenting our findings so that others may test them. In summary, our current reasoning about our preliminary findings is that families which manifest se-

vere bipolar disorder may be more likely to have a monogenic form of the disorder, whereas families with a mixture of both bipolar and unipolar phenotypes which have clinically milder illness may be more likely to have a multigenic form of bipolar I disorder.

We have attempted to reduce the number of sporadic cases of depression by requiring that our subjects with unipolar disorder have recurrent major depressions. We have also looked at indexes of diagnostic stability for our unipolar subjects (24). Our unipolar subjects had an average of 3.4 (SD=1.2) episodes of depression and 6.5 (SD=1.2) of a possible eight RDC depressive symptoms in their most severe episodes. Fifty percent were treated with medications for their depressions. While we cannot be sure that recurrent depression of this severity always represent genetic forms of depression, we hope that this requirement will eliminate many sporadic cases (25, 26).

We have tried to detect phenocopies by searching for possible organic causes of major affective disorder in affected family members. If the proband appeared to have a possible organic affective disorder, he or she was designated as an unsuitable proband and the family was not accepted into the study. If the disorder of an affected family member appeared to have an organic etiology, that individual was designated as having an uncertain phenotype and will not be included in the linkage analysis. If this individual were a sib or parent of the unaffected parent, this would not result in the family's being classified as probably bilineal. A true phenocopy in the sib or parent of the unaffected parent, however, would result in false labeling of the family as probably bilineal. It is hoped that the prevalence of these phenocopies is low.

Thus, we have made a serious effort to designate sporadic or nongenetic depression as an uncertain or unknown phenotype. The issue of whether even recurrent cases of depression should be considered genetic cases of depression will be reviewed before linkage analysis.

Strategies for Ascertaining Unilineal Families

Because of the current limitations of genetic linkage methods and nonreplication of recent linkage findings for bipolar I disorder, a cautious approach to family selection is warranted. Only a set of clearly unilineal families will allow a test of the hypothesis that bipolar I disorder can be inherited through mendelian dominant transmission. On the basis of our experience, we recommend several strategies for ascertaining unilineal bipolar I families.

Two-step method for detecting bilineality. The first step consists of taking an extensive family history of both parents' families. A family that appears to be unilineal moves on to step 2 (direct examination); the parents are interviewed first, followed by the sibs of the proband, then the aunts, uncles, and grandparents. This requires that the unaffected parent and some of his or her sibs and/or parents be available for direct interview. If a parent, aunt, uncle, or grandparent on the "unaf-

ected" side of the family is found by interview to be affected, we recommend that the family be designated as probably bilineal and excluded from the sample for linkage analysis. The probably bilineal families can be used in clinical comparisons with the unilineal families. In addition, after some of the genes for bipolar disorder have been found, these families will be of great interest for genetic studies.

Other authors have given general prescriptions for detecting bilineality to exclude such families from linkage analyses (6, 7). However, to our knowledge, no fully operationalized methods (including who must be directly interviewed and which phenotypes must be excluded) have been published to date. We have not compared our method with other methods. A pragmatic test of our method will be undertaken in the planned linkage analysis; however, comparative assessments of methods for detecting bilineality would also be useful.

Narrow definitions of phenotypes. We recommend very narrow definitions of affected and unaffected status. A high threshold for calling a parent of a proband unaffected is warranted in order to identify and exclude potentially bilineal families. It is also recommended that any psychopathology in the parents, aunts and uncles, and grandparents of the proband be described and documented in order to quantitatively assess the risk that they are genetically affected.

Using a high threshold for designating sibs as affected will decrease the number of phenocopies (false positives), which may have a major effect on the linkage analysis.

Relatives who are not clearly affected but who have conditions that have been associated with the bipolar phenotype should be designated as having uncertain phenotypes (3, 7) and followed longitudinally.

Selection of families with bipolar disorder in at least two generations. While it may be that only a minority of bipolar I cases may result from dominant transmission of a single gene, it is most conservative to look first at families which appear to be of this type. Selection of families with bipolar I disorder in at least two generations should increase the probability of finding unilineal families and of finding mendelian forms of bipolar I disorder.

Family structure requirement. Unilineal families with one affected parent and only one affected sib in addition to the proband are highly informative. This family structure provides almost as much linkage information as those with three affected sibs (27) and may be less likely to be bilineal.

Systematic ascertainment of families. We studied a number of self-referred families with three or more affected sibs, and almost all these families were bilineal. Therefore, we recommend that families be ascertained by systematic screening of clinical services.

CONCLUSIONS

The mode of inheritance of bipolar I disorder is unknown. While there may be mendelian dominant forms

of the disorder, they may be uncommon. If the current searches for mendelian forms of the disorder are to have the best chance of success, an adequate resource of unilineal families must be studied with DNA markers spanning the entire genome.

Finding suitable unilineal families for genetic linkage studies is a labor-intensive process requiring extensive screening of patient populations in treatment facilities. However, the ascertainment and careful clinical study of a sufficiently large number of such families should increase the probability of positive linkage findings and decrease the probability of nonreplication of positive findings.

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Schizoaffective Disorder and Affective Disorders With Mood-Incongruent Psychotic Features: Keep Separate or Combine? Evidence From a Family Study

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Objective: This study investigated whether the distinction between schizoaffective disorder and affective disorders with mood-incongruent psychotic features as described in DSM-III-R is reflected by aggregation of schizophrenia in the families of probands with the former disorder and aggregation of affective disorders mainly among the relatives of probands with the latter type of disorders. **Method:** The probands were 118 inpatients with definite lifetime diagnoses of DSM-III-R schizoaffective disorder or a major mood disorder with incongruent psychotic features according to structured clinical interviews. Diagnostic information on 475 of the probands' first-degree relatives was gathered through direct interviews (with 80% of the living first-degree relatives) or the family history approach. The rates of affective and psychotic disorders among these relatives were then compared with those among the relatives of a comparison group of 109 interviewed individuals from the general population who were matched on sociodemographic factors to the inpatient probands. **Results:** With regard to the familial aggregation of schizophrenia, the DSM-III-R distinction emerged as valid. However, the risk of unipolar affective disorders was enhanced in the families of all of the subgroups of patients studied. The unipolar/bipolar distinction in both DSM-III-R diagnostic groups was reflected by distinct patterns of bipolar disorders in the relatives. **Conclusions:** The results partly support the DSM-III-R dichotomy of schizoaffective disorder and affective disorders with mood-incongruent psychotic features. Although the differences between these two diagnostic groups were significant, the magnitude of the differences remained relatively modest.

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There is broad agreement that the lifetime diagnosis of patients with a lifetime comorbidity of pure affective episodes (manic episode/major depressive episode) and pure schizophrenic episodes should adhere to the hierarchical principle that schizophrenia takes priority. On the other hand, the classification of the co-occurrence, within the same episode, of a major affective syndrome and a psychotic syndrome that is not due to the affective syndrome is highly controversial. Different criteria (e.g., which of the two syndromes preceded the other one; the relative duration of temporal overlap; preponderance of symptoms versus severity of symptoms) are considered to be crucial by the various diagnostic

schedules. A variety of diagnostic classifications with various degrees of inclusiveness have been proposed. The Research Diagnostic Criteria (RDC) (1) suggest three main diagnostic categories (affective, schizoaffective, and schizophrenic disorders), with one diagnostic category, schizoaffective disorder, for episodes with two syndromes showing considerable temporal overlap. The RDC further recommend subdividing this diagnosis according to the relative preponderance of a particular syndrome during the episode, resulting in a schizophrenic and an affective subtype of schizoaffective disorder. The subclassification according to affective and schizophrenic syndromes was constructed in order to dissolve the heterogeneous group of schizoaffective disorders (2, 3) into two homogeneous subgroups. The support for this suggestion from family study data, however, has been ambiguous. On the one hand, Baron et al. (4) were able to discriminate probands with schizoaffective disorder who had an elevated risk of schizophrenic disorders but no increased

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risk of affective disorders from those with the reversed pattern by subdividing the probands as recommended by the RDC. On the other hand, some family studies of schizoaffective disorder that used this manner of subtyping revealed more similarities than differences between these two subgroups with regard to the diagnostic patterns of familial aggregation (5).

DSM-III-R was a new attempt to split the group of patients identified by the RDC as having schizoaffective disorder by redefining the distinction proposed in the RDC (the RDC affective subtype corresponding to *DSM-III-R* mood disorders with mood-incongruent psychotic features and the RDC schizophrenic subtype corresponding to *DSM-III-R* "true" schizoaffective disorder) (6). These definitions were more precisely worked out than the definitions of the RDC subtypes and focus on a required minimum duration of psychotic symptoms in the absence of affective syndromes. In contrast to the RDC's three main categories (affective, schizoaffective, and schizophrenic disorders) *DSM-III-R* was oriented toward Kraepelin's dichotomy by splitting the range of overlapping affective and psychotic conditions into two subgroups belonging to the two main categories: those which are allocated to affective disorders (termed mood disorders with mood-incongruent psychotic features) and those allocated to psychotic disorders (schizoaffective disorder). The crucial differential criterion is whether the mood-incongruent psychotic features mainly occur when the criteria for a major affective syndrome are fulfilled (affective disorder with psychotic features) or whether psychotic features are also present for 2 weeks or longer after the affective syndrome has remitted or before the affective syndrome will become apparent (schizoaffective disorder).

The validity of the RDC definition of schizoaffective disorder is supported by family studies that were able to demonstrate familial aggregation of schizoaffective disorder. Two family studies of probands with affective as well as psychotic syndromes according to *DSM-III-R* criteria have been published up to now (7, 8); the study by Maj et al. (8) presented data on unipolar depression only, not on bipolar patients. Both studies are very clearly in support of *DSM-III-R*. Limitations inherent in these two *DSM-III-R*-based studies suggest that their conclusions be considered as preliminary. The study by Kendler et al. (7) was an evaluation of the material collected by the Iowa 500 study; the authors conceded the limitation of this approach in their article. The study by Maj et al. (8) is unusual among the universe of family studies using the Schedule for Affective Disorders and Schizophrenia—Lifetime Version (SADS-L) in that it reported extremely low rates of affective disorders in families of control subjects and of probands with affective disorders. In particular, the lifetime risks among families of control subjects were substantially lower than those in all epidemiological surveys and in comparison groups of family studies using the same instrument (SADS-L). (There was, for example, an epidemiological survey that used the same interview in the same country and reported a 1-year prevalence rate of 8.5%

for mood disorders [9]). Furthermore, schizophreniform disorder (*DSM-III-R*) and other psychotic disorders (including schizoaffective disorder) were not recorded for family members. Therefore, replications of the results found and the conclusions drawn by Kendler et al. and Maj et al. are needed.

This report refers to a family study that recruited inpatients and their families irrespective of their diagnoses. Patients with *DSM-III-R* diagnoses of affective disorders with mood-incongruent psychotic features or schizoaffective disorder and their families were selected and compared, grouped according to their *DSM-III-R* diagnoses, with subjects recruited in the general population and their families. Probands who had affective disorders with mood-congruent psychotic features and their families were not included in the study. Taking into account the bipolar/unipolar distinction, we tested the hypothesis inherent in *DSM-III-R* that families of probands with affective disorders with psychotic features are at greater risk for affective disorders but not for schizophrenia, whereas schizoaffective probands might carry an elevated familial risk of schizophrenia. Bipolar subjects who reported full-blown manic episodes were included; those who had hypomanic episodes only were excluded from the study.

METHOD

Psychopathological and Final Diagnostic Assessment

The probands and their relatives were directly interviewed with an extended version of the Schedule for Affective Disorders and Schizophrenia—Lifetime Version Modified for the Study of Anxiety Disorders (SADS-LA) (10). The SADS was originally based on the RDC but also includes the criteria in the mood disorders section of *DSM-III-R*. In order to classify psychotic disorders also according to *DSM-III-R*, the corresponding sections on schizophrenia and psychotic disorders of the Structured Clinical Interview for *DSM-III-R* (SCID) (11) were applied. Schizotypal personality disorders were assessed by means of the personality disorders module of the Structured Clinical Interview for *DSM-III-R* (SCID-II) (12).

We used the family history approach (13) to ask the relatives of probands about psychiatric syndromes in the other members of the family being assessed (with exception of the proband). The family history method provides a semistructured interview for RDC and *DSM-III-R* diagnoses of major affective, schizoaffective, and schizophrenic disorders and of anxiety disorders, alcoholism, drug abuse, and eating disorders. Minor disorders and personality disorders are not included.

The personal interviews and the family history assessments were conducted by 11 research assistants (advanced medical students with clinical experience in psychiatry or young physicians) after a common training program of at least 20 sessions with all instruments to

be used. Test-retest reliabilities for all *DSM-III-R* diagnoses discussed in this article were tested separately and were acceptable (κ values higher than 0.75). The reliability study has been published separately (14).

The final diagnostic assessment according to the RDC and the *DSM-III-R* criteria was performed by two experienced psychiatrists (W.M. and R.H.), who combined the information obtained by personal interview (if available), the family history information obtained from all sources available, and the case notes (if present) and made a final diagnosis using the RDC and *DSM-III-R* manuals. The same procedure was applied to both probands and relatives. The best-estimate diagnoses (15) were allocated independently to probands and relatives. The diagnostic assessments we report were lifetime diagnoses made by following a hierarchical procedure: schizophrenia has priority over schizoaffective disorder, which is followed by bipolar and then by unipolar major affective disorders.

Recruitment of Probands

Patient probands. The families under study were derived from an extensive family study including probands with all kinds of affective disorders, schizophrenia, and other psychotic disorders. Inpatients consecutively admitted to the psychiatric hospital of the University of Mainz between January 1988 and August 1989 and aged between 20 and 70 years were first screened by the treating physician for somatic factors causing psychiatric distress. Patients without an established organic etiology, without a history of seizures, and without dementia were further screened by means of the SADS-LA. Patients reporting a previous or current episode of any psychotic or major affective disorder according to the RDC or *DSM-III-R* criteria were included in the family study if at least one living first-degree relative agreed to be personally interviewed with respect to his or her and the family's psychiatric history and status. Additionally, patients with a history of the above-mentioned disorders as evidenced by case reports and by clinical judgment were included even if they could not be interviewed during their stay in the hospital because of the severity of their psychological impairment. For all members of this subgroup it was required that at least one living first-degree relative be accessible for the personal interview.

Five hundred twenty-five patients were selected as probands for the family study. Only probands with unambiguous evidence of mood-incongruent psychotic features and hence a *DSM-III-R* diagnosis of either schizoaffective disorder or a major affective disorder with mood-incongruent, not mood-congruent, psychotic features were selected for this report. Only if both clinicians deciding on the best-estimate diagnoses agreed on the definite presence of either of these two disorders, and if they were able to rule out unambiguously the diagnosis of schizophrenic disorders or affective disorders without mood-incongruent psychotic features, was the proband included in the sample. Of the

original group of 525 patients, 140 fulfilled these requirements and presented with a definite lifetime diagnosis of either schizoaffective disorder or a major affective disorder with mood-incongruent psychotic features according to the *DSM-III-R* criteria.

To draw valid conclusions from comparisons of diagnostic subtypes by familial loading, diagnostic certainty in subtyping the probands and consistency in applying the diagnostic criteria across subtypes are crucial requirements. By adhering to these principles, we excluded 22 additional patients with either of the disorders being studied (and their families) from the group of 140 patients and their families for the following reasons. 1) Twelve patients reported episodes with overlapping psychotic and affective syndromes, but the available information (including medical records) was not sufficient or unequivocal enough to decide with certainty between schizoaffective disorder and mood disorder. It was not possible to determine whether delusions and/or hallucinations were present for 2 weeks or longer without prominent affective symptoms. 2) Ten patients fitted the *DSM-III-R* requirements for schizoaffective disorder or a mood disorder with incongruent psychotic features but also reported hypomanic episodes accompanied by incongruent psychotic features without ever having suffered from a full-blown manic episode (bipolar II probands). Families of these probands were not included, as the *DSM-III-R* classification is inconsistent at this point: bipolar II probands who have major depressive episodes with mood-incongruent psychotic features may be considered to have bipolar disorder not otherwise specified. However, *DSM-III-R* does not recognize bipolar II schizoaffective disorder and classifies bipolar II probands with episodes of schizoaffective disorder, depressive type, as having unipolar schizoaffective disorder, depressive type, ignoring the bipolar condition. Exclusion of bipolar II probands and their families enabled a consistent application of the unipolar/bipolar dichotomy to psychotic mood disorders and schizoaffective disorder.

Diagnostic information from 475 first-degree relatives (aged 18 years or older) of the remaining 118 probands with schizoaffective disorder or mood disorders with incongruent psychotic features was gathered by either the family history method or the family study method.

Comparison probands. One hundred nine comparison probands with at least one living and accessible first-degree relative were recruited from the general population of the same area from which the inpatient probands came. The sampling scheme was based on the socioecographic characteristics of a randomly drawn subsample of the index patients (probands), to which the comparison group probands were matched pairwise by sex, age, educational level, occupational status, and residential district. The recruitment of the comparison subjects was assisted by a professional marketing institute. As recommended by Tsuang et al. (16) and Kendler (17), these probands were not screened for diagnoses. Information was obtained from 432 relatives

TABLE 1. Numbers, Ages, and Gender Composition of Three Groups of Probands and Their First-Degree Relatives

Group/Variable	Proband Group				Comparison Subjects (N=109)
	Schizoaffective Disorder		Affective Disorders With Incongruent Psychotic Features		
	Bipolar Type (N=21)	Unipolar Depressive Type (N=23)	Bipolar Disorder (N=34)	Unipolar Major Depression (N=40)	
Probands					
Age (years)					
Mean	38.4	39.9	37.6	38.6	38.6
SD	8.5	10.1	8.2	9.8	10.9
Male sex					
N	9	8	13	13	54
%	42.9	34.8	38.2	32.5	49.5
Relatives					
Total number	85	87	138	165	432
Number living	70	70	112	142	370
Number interviewed	55	58	90	110	292
Interviewed relatives					
Age (years)					
Mean	44.5	44.9	45.4	44.0	39.8
SD	16.5	18.3	14.3	15.9	16.9
Male sex					
N	26	27	43	57	142
%	47.3	46.6	47.8	51.8	48.6

(aged 18 years or older) of the comparison probands by the family study or the family history method.

Investigation of Family Members

Diagnostic information on probands' first-degree relatives who refused to be interviewed or who were dead was obtained by the family history method from at least one informant per family. The interviewers were blind to the diagnostic status of the probands. We also collected medical records if we had the consent to do so.

Table 1 displays the characteristics of the probands and the relatives studied.

Statistical Methods

The presentation of familial rates combines data on relatives who were personally interviewed with data on those for whom only family history information was available for the following three reasons. 1) The ratios of personally interviewed relatives were very similar across groups (table 1). 2) The rate of affected relatives (combining all disorders) obtained by the family history method was lower than the rate yielded by the family study method, but not significantly so ($\chi^2=2.2$, $df=1$, $p>0.05$) in any of the five groups of relatives compared. 3) The majority of relatives who were not interviewed personally were classified by systematically collected information from multiple informants, not just a single one.

Since *DSM-III-R* schizoaffective disorder and affective disorders with mood-incongruent psychotic features do not differ in the distribution of their ages at

onset (in the life table analysis comparing age at onset of all probands or relatives with schizoaffective disorder to age at onset of those with psychotic mood disorders, $\chi^2=0.4$, $df=1$, $p>0.10$), and since the distribution of the current ages of the probands and relatives did not differ among the schizoaffective, the psychotic affective, and the comparison groups (table 1), age correction was not necessary for comparing the proband groups under study. Therefore, we simply report the relative frequencies of disorders (in percents) in the families of the various proband groups. The familial rates for the proband groups were compared by means of chi-square tests (two-tailed); there was 1 degree of freedom unless otherwise indicated.

Because schizophrenia and related disorders are rare in community samples, it is likely that some cells in contingency tables will be empty or show only a very low relative frequency. Thus, a correction procedure for the chi-square test is required; we selected the pseudo-Bayesian approach (18) for this purpose.

RESULTS

Table 2 displays the relative frequencies of psychotic and affective disorders in families by proband type. All disorders under consideration were more frequent in the families of all patient groups than in the families of the healthy comparison probands. When combining the unipolar/bipolar subgroups of probands and relatives, we found that the following disorders were significantly more common among relatives of probands with schizoaffective disorder than among relatives of the comparison subjects: schizophrenia ($\chi^2=6.4$,

TABLE 2. Morbid Risks for DSM-III-R Psychotic Disorders and Affective Disorders Among First-Degree Relatives of Three Groups of Probands

Diagnosis of Relatives	Proband Group									
	Schizoaffective Disorder				Affective Disorders With Incongruent Psychotic Features				Comparison Subjects (432 Relatives)	
	Bipolar Type (85 Relatives)		Unipolar Depressive Type (87 Relatives)		Bipolar Disorder (138 Relatives)		Unipolar Major Depression (165 Relatives)			
			N	%			N	%		
N	%	N	%	N	%	N	%	N	%	
Schizophrenia										
Total	3	3.5	2	2.3	3	2.2	2	1.2	2	0.5
With affective syndromes	2	2.4	1	1.1	1	0.7	2	1.2	1	0.2
Without affective syndromes	1	1.2	1	1.1	2	1.4	—	—	1	0.2
Schizophreniform disorder										
Total	1	1.2	1	1.1	—	—	2	1.2	—	—
With affective syndromes	1	1.2	1	1.1	—	—	1	0.6	—	—
Without affective syndromes	—	—	—	—	—	—	1	0.6	—	—
Schizoaffective disorder										
Total	2	2.4	2	2.3	2	1.4	2	1.2	1	0.2
Bipolar type	1	1.2	1	1.1	1	0.7	—	—	—	—
Unipolar depressive type	1	1.2	1	1.1	1	0.7	2	1.2	1	0.2
Other DSM-III-R psychotic disorders	—	—	2	2.3	1	0.7	2	1.2	2	0.5
Affective disorders with incongruent psychotic features										
Total	3	3.5	1	1.1	4	2.9	3	1.8	2	0.5
Bipolar disorder	2	2.4	—	—	2	1.4	1	0.6	—	—
Unipolar major depression	1	1.2	1	1.1	1	0.7	2	1.2	2	0.5
Affective disorders without incongruent psychotic features										
Total	17	20.0	12	13.8	27	19.6	25	15.2	32	7.4
Bipolar disorder	4	4.7	1	1.1	7	5.1	2	1.2	4	0.9
Unipolar major depression	13	15.3	11	12.6	20	14.5	23	13.9	28	6.5
Minor affective disorders										
Total	2	2.4	1	1.1	4	2.9	2	1.2	7	1.6
Cyclothymia	1	1.2	—	—	3	2.2	1	0.6	4	0.9
Dysthymia	1	1.2	1	1.1	1	0.7	1	0.6	3	0.7

$p=0.01$), schizophreniform disorder ($\chi^2=4.6$, $p=0.02$), schizoaffective disorder ($\chi^2=6.4$, $p=0.01$), psychotic mood disorders ($\chi^2=4.4$, $p=0.02$), nonpsychotic unipolar mood disorder ($\chi^2=8.9$, $p<0.01$), and nonpsychotic bipolar mood disorder ($\chi^2=3.2$, $p=0.05$). The following disorders were more common among relatives of probands with major mood disorders with incongruent psychotic features: schizophrenia ($\chi^2=2.5$, $p=0.05$), schizophreniform disorder ($\chi^2=2.2$, $p=0.07$), schizoaffective disorder ($\chi^2=3.1$, $p=0.05$), psychotic mood disorders ($\chi^2=4.8$, $p=0.02$), nonpsychotic unipolar mood disorder ($\chi^2=11.2$, $p=0.001$), and nonpsychotic bipolar mood disorder ($\chi^2=4.2$, $p=0.03$). The familial rates of minor affective disorders (if a hierarchical rule is applied to the diagnoses) were not different between either group of patients and the comparison subjects (schizoaffective disorder, $\chi^2=0.0$, $p>0.10$; affective disorders with mood-incongruent psychotic features, $\chi^2=0.2$, $p>0.10$).

In the comparison of the schizoaffective disorder and the psychotic mood disorder proband groups for familial rates of nonaffective psychotic disorders, divergent trends appeared (table 2). The risk of schizophrenia as well as schizoaffective disorder was nearly twofold

higher for the family members of the schizoaffective proband group than for the relatives of the affective disorder proband group, but not significantly so ($\chi^2=0.4$, $p>0.10$, and $\chi^2=0.3$, $p>0.10$, respectively).

Five cases of DSM-III-R schizotypal personality disorder (1.6%) without psychotic disorder (i.e., without schizophrenia or schizophreniform, schizoaffective, or other psychotic disorders) were found among the directly interviewed relatives of the patients with schizoaffective disorder or psychotic mood disorders, whereas two cases (0.7%) were found among the interviewed relatives of the comparison subjects (data not shown). Schizotypal personality disorder was primarily observed in the families of probands with unipolar disorder: two cases (3.4%) among the relatives of probands with unipolar schizoaffective disorder, two cases (1.8%) among the relatives of probands with psychotic unipolar major depression, and one case (1.8%) among the relatives of bipolar schizoaffective probands.

Table 2 gives information about the nature of schizophrenia and schizophreniform disorder in the families of probands with schizoaffective or psychotic mood disorders. Only half of the schizophrenic relatives also reported a previous depressive, manic, or schizoaffective

tive episode. No consistent pattern emerged when the proband groups were compared by the percentages of schizophrenic/schizophreniform relatives who showed comorbid major affective syndromes on a lifetime basis.

The families of patients with schizoaffective disorder, as well as those of patients with mood disorders with incongruent psychotic features (ignoring the unipolar/bipolar dichotomy) were at significantly greater risk for any subtype of mood disorder than the families of the comparison subjects ($\chi^2=14.6$, $p=0.001$, and $\chi^2=20.4$, $p=0.001$, respectively). However, the families of the two types of patient probands did not significantly differ in their rates of affective disorders ($\chi^2=0.0$, $p>0.10$).

An additional feature of the data displayed in table 2 is most remarkable: bipolar affective disorders and bipolar schizoaffective disorder (i.e., conditions with at least a full manic syndrome at one time for at least 8 days) predominantly aggregated in the families of probands with bipolar affective disorders or bipolar schizoaffective disorder. The elevation of the risk for bipolar disorder was significant in the families of both proband types ($\chi^2=14.3$, $p=0.001$, and $\chi^2=14.7$, $p=0.001$, respectively). Neither the families of the unipolar schizoaffective proband group nor the families of the unipolar affective disorder proband group (with mood-incongruent psychotic features) were at greater risk for bipolar affective or bipolar schizoaffective disorders ($\chi^2=1.4$, $p>0.05$, and $\chi^2=0.9$, $p>0.05$, respectively).

The risk for unipolar depression and unipolar schizoaffective disorder was enhanced in the families of patients with any subtype of disorder compared to the families of the comparison subjects. The elevation of the risk of unipolar major depression was significant for the families of probands with psychotic unipolar depression ($\chi^2=8.5$, $p=0.01$) and those with unipolar schizoaffective disorder ($\chi^2=9.0$, $p=0.01$) as well as for the families of probands with psychotic bipolar disorder ($\chi^2=4.8$, $p=0.02$) and those with bipolar schizoaffective disorder ($\chi^2=9.8$, $p=0.01$). The link of bipolar schizoaffective disorder and of psychotic bipolar affective disorder to schizophrenia was as strong as the link of unipolar schizoaffective disorder and of unipolar affective disorder to schizophrenia. The familial rates for schizophrenia or schizophreniform disorder were not different for the relatives of the unipolar and the bipolar proband groups ($\chi^2=0.1$, $p>0.10$).

DISCUSSION

The global rate of occurrence of disorders characterized by an overlap of affective and schizophrenic syndromes in the families in this study is comparable to that in other reports. Previous studies, summarized by Gershon et al. (19), found morbid risks, depending on particular subtypes, between 0.0 (20) and 7.4 (21) for broadly defined schizoaffective disorder. If we combine the risk among relatives for *DSM-III-R*-defined schizoaffective disorder and affective disorders with mood-in-

congruent psychotic features, the familial rates in our study vary between 3% (five of 165 relatives of probands with unipolar depression with mood-incongruent psychotic features) and 6% (five of 85 relatives of probands with schizoaffective disorder, bipolar type), which is within the range spanned by previous studies.

The distinction between schizoaffective disorder and affective disorders with mood-incongruent psychotic features as proposed by *DSM-III-R* received some support in our family study: 1) schizophrenia and related conditions were more closely related to *DSM-III-R* schizoaffective disorder than to psychotic affective disorders, and 2) *DSM-III-R* schizoaffective disorder was more common in families of probands with this condition than in families of probands with affective disorders. The first finding is in agreement with the two other reports on this *DSM-III-R* distinction, those of Kendler et al. (7) and Maj et al. (8), and with the earlier report by Baron et al. (4). The second finding is also in agreement with Kendler et al. (7) and—if the differences between the RDC and *DSM-III-R* criteria are ignored—with Baron (4), whereas schizoaffective relatives are not mentioned by Maj et al. (8). Both of these findings are at variance with those of Angst et al. (5), who found the same familial background for the schizophrenic and the affective subtypes of a broadly defined group of patients with affective as well as psychotic syndromes. However, because the familial loading varied across the groups of probands in our study, it does not support the combination of the four subgroups of patients under a unitary diagnostic category (schizoaffective disorder) as is recommended by the RDC.

However, substantial disagreement with Baron et al. (4) and—for the unipolar subtypes—with Maj et al. (8) is also apparent from our family study. As previously reported by Angst et al. (5), we found schizoaffective disorder and psychotic affective disorders to be related to both schizophrenia and nonpsychotic affective disorders. As far as nonpsychotic unipolar major depression is concerned, this finding also contradicts the reevaluation of the Iowa 500 study by Kendler et al. (7), but it does not do so for nonpsychotic bipolar disorder. The risk for nonpsychotic bipolar disorder was elevated in the families of schizoaffective probands (defined by *DSM-III-R* criteria) in the report by Kendler et al. Consequently, the Iowa 500 data also indicate some link between a schizophrenia-type variant of schizoaffective disorder and affective disorders (nonpsychotic), even though Kendler et al. did not stress this relationship in their discussion.

Beyond the similarity of our results to those obtained by Angst et al. (5), the features moderating the variation of familial risks across the various subtypes of probands differ between the two studies. Two aspects are most noticeable in this respect.

1. We found that the familial loading for affective disorders varies along the unipolar/bipolar dichotomy; the schizoaffective/psychotic affective distinction had no impact on the variation of familial rates of affective disorders. Angst et al. (5) reported that neither the bipolar/

unipolar nor the schizo-dominant/affect-dominant distinction was relevant in this respect. Evidence from the literature mainly favors our conclusion: all studies (except that of Angst et al.) report a strong relationship between bipolar schizoaffective disorder and bipolar affective disorder (19, 22). The majority of studies also report virtually equal familial rates of nonpsychotic unipolar depression for unipolar and bipolar schizoaffective proband groups.

2. Our data reveal that the familial risk for schizophrenia is higher in the more schizophrenic than in the more affective proband group; the bipolar/unipolar distinction was not associated with different familial risks for schizophrenia. Angst et al. (5) found no impact of the schizo-dominant/affect-dominant distinction in this respect, but they reported the unipolar depressive subtype to be more closely related to schizophrenia than the bipolar subtype. At this point our results receive support from the literature. All family studies (except the one by Angst et al.) that have subdivided a broadly defined group of schizoaffective conditions (including mood disorders with incongruent psychotic features) into a schizophrenic/affective type dichotomy found the more schizophrenic subtype to be more closely linked to schizophrenia than the more affective subtype. The evidence for a particularly close relationship between the bipolar subtype and schizophrenia is less strong (22).

A peculiar finding of our study was the familial homotypy observed for the combination of bipolar affective and bipolar schizoaffective disorder. The exclusion of probands with hypomania but without a lifetime history of mania might have contributed to this homogeneous pattern. Previously, Baron et al. (4) reported a similarly distinct pattern for the combined bipolar group. On the other hand, Kendler et al. (7) and Gershon et al. (19) found a greater rate of nonpsychotic bipolar disorder in families of probands with unipolar schizoaffective disorder or psychotic affective disorders who never presented with manic syndromes. We cannot offer a convincing explanation for these divergent results; we can only exclude the impact of the differences between different classification schedules, since Baron et al. (4) and Gershon et al. (19) used the RDC, whereas Kendler et al. (7) used *DSM-III-R*. Furthermore, the follow-up period for the probands examined by Kendler et al. lasted for decades, and therefore in that particular study, the unipolar cases were truly unipolar and not hidden bipolar cases.

It has not been established whether schizoaffective disorder represents a particular diagnostic entity or a variant of either schizophrenia or affective disorders (22). Our study found a higher rate of a particular diagnostic subgroup in the families of probands who belonged to the same subgroup. However, there were much higher familial rates of affective or schizophrenic/schizophreniform disorders in both subgroups under study. This statement remains true if the four diagnostic subgroups we studied are collapsed into one group. Most investigators have been motivated by similar observations to deny that schizoaffective disorder is

a distinct form of psychosis (23). However, the validity of this conclusion depends on the relative base rates of the three conditions (schizophrenia, affective disorders, and the combination of the two) in the general population. In our opinion, this conclusion is not justified, since affective disorders are clearly very much more common in the community than both of the other kinds of disorders and since the relation between the prevalences of schizoaffective disorder and schizophrenia/schizophreniform disorder in the general population is not known (and is hard to estimate because both conditions are rare). Therefore, the problem of whether schizoaffective disorder in a broad or in a narrow sense defines a distinct diagnostic category remains unsettled. However, schizoaffective disorder as well as psychotic affective disorders are linked with similar strength to nonpsychotic affective disorders.

The present family study backs up the conclusions drawn from follow-up studies of similar proband groups. Coryell et al. (24, 25) found that diagnostic distinctions between schizophrenia-type and affective-type symptoms and distinctions by temporal dissociation between psychotic and affective symptoms were most consistent and represented strong predictors of sustained delusional outcome. In contrast to the present and other family studies, follow-up studies lend only limited support to the validation of the distinction between unipolar and bipolar subtypes (26).

CONCLUSIONS

Differences in familial loading for schizophrenia, schizophreniform disorder, and schizoaffective disorder are one reason to keep schizoaffective disorder and mood disorders with incongruent psychotic features as separate diagnostic groups. However, since these differences are modest and more of a quantitative than of a qualitative nature, it is hard to accept that the boundary between these two diagnostic groups represents the demarcation line between the two major *DSM-III-R* diagnostic categories of schizophrenic and mood disorders. It is noteworthy in this context that only probands with definite mood-incongruent psychotic features and schizoaffective disorder or mood disorder with incongruent psychotic features were included. Consequently, the failure to find a stringent delineation between the diagnostic categories with regard to their familial loading cannot have been due to probands with uncertain diagnoses. The view that *DSM-III-R* schizoaffective disorder and *DSM-III-R* psychotic affective disorders are located on a continuum ranging from schizophrenic to nonpsychotic mood disorders is, therefore, more appropriate than allocating them to two distinct nosological entities. Alternatively, the two diagnostic groups under study might indicate two subtypes of a broadly defined concept of schizoaffective disorder representing a separate diagnostic category located between schizophrenia and affective disorders, as has been proposed by the RDC.

It is beyond the scope of this article to evaluate a third alternative view: the difference between the two *DSM-III-R* diagnoses under study might be due to differences in the qualifying conditions. Only conditions that cross-sectionally reveal a full schizophrenic syndrome qualify for *DSM-III-R* schizoaffective disorder if the exclusion criteria and temporal requirements are ignored. *DSM-III-R* mood disorders with mood-incongruent psychotic features may fail to fulfill the criteria for a full-blown *DSM-III-R* schizophrenic syndrome. Therefore, a plausible explanation of our results might be that the more similar a proband's psychopathological syndrome is to schizophrenia (cross-sectionally), the closer will be the familial link to schizophrenia, irrespective of the temporal overlap with affective syndromes.

Besides the reevaluation of the Iowa 500 study by Kendler et al. (7), this family study is the second in the literature to test the subdivision of the *DSM-III-R* categories of schizoaffective disorder and psychotic affective disorders by the unipolar/bipolar dichotomy. Both studies agree that this subdivision is a valid one; elevated rates of bipolar conditions are found only if the probands belong to a bipolar group. We are further in agreement with the reevaluated Iowa 500 study; in both reports *DSM-III-R* bipolar schizoaffective disorder is as closely linked to schizophrenia by familial risk figures as is unipolar schizoaffective disorder. In contrast to this conclusion, studies exclusively relying on the RDC suggest that bipolar schizoaffective disorder—but not unipolar schizoaffective disorder—is more a variant of affective than of schizophrenic disorders (23). The requirement in *DSM-III-R*, but not in the RDC, that schizoaffective disorder must meet the cross-sectional criteria of a full-blown schizophrenic syndrome at one time might explain these discrepant results.

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Reliability of Best-Estimate Diagnosis in Genetic Linkage Studies of Major Psychoses: Results From the Quebec Pedigree Studies

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Objective: Diagnostic classification and reliability are critical in genetic linkage studies of schizophrenic and bipolar disorder. To establish an optimal diagnostic procedure, the authors drew 13 methodological elements from 38 major linkage studies and workshop reports. They determined reliability for a consensus best-estimate diagnostic method based on these 13 features. **Method:** Each of 59 subjects from several large multiplex pedigrees, densely affected by either schizophrenia or bipolar disorder, received a best-estimate diagnosis from unblind diagnosticians in the field and also from a panel of four research psychiatrists who were blind to the proband's and relatives' clinical status. The best estimate was based on personal diagnostic interviews, all available medical records, and family history data. **Results:** The diagnostic concordance between the field team and the blind psychiatric board yielded 78% to 90% agreement for the whole sample ($\kappa=0.83-0.88$) and 71% to 87% agreement for the subjects given field diagnoses ($\kappa=0.76-0.83$). The diagnoses made by the unblind field diagnosticians were biased toward a greater severity (or certainty) level in the diagnostic hierarchy (schizophrenia or bipolar) and more consistency with the most prevalent diagnosis affecting the pedigree. **Conclusion:** Since several previous linkage studies used diagnoses made by diagnosticians who were not blind to the status of the probands and the relatives or did not use a consensus best-estimate diagnosis, further reliability studies of different aspects of the best-estimate method and of its effect on linkage studies are needed. Such research is imperative given the serious impact of diagnostic misclassifications on genetic linkage results.

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The linkage studies searching for a genetic marker for schizophrenia or bipolar disorder have yielded inconsistent results. Differences in diagnostic methods

and reliability are assuredly a major source of discrepancies between findings (1-4 and unpublished 1989 paper by T. Reich). Heterogeneity in the genetic etiology of the disorders, sampling differences, and difficulties in detecting phenocopies are additional causes for the differences in findings.

In the present paper we 1) review the previous major reports of linkage studies in terms of the diagnostic procedures in use, 2) derive methodological priorities from these prior works, 3) describe the best-estimate diagnostic method used in the Quebec pedigree studies, and 4) provide reliability data on our procedure.

PREVIOUS STUDIES

We reviewed 38 major studies published since 1980 and report on the presence or absence of findings of linkage between either schizophrenia (16 studies) or bi-

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polar disorder (22 studies) and different genetic and biological markers. The main finding from this review is the striking discrepancies between reports in terms of the diagnostic methods or, more commonly, the lack of details about these procedures, even in the most recent reports. This lack of detail often makes comparisons of procedures between studies very difficult and is inevitably due to the fact that several of these studies were designed before the development of the current tighter and more comprehensive epidemiological procedures (5-7). Tables 1 and 2 compare the studies according to 13 characteristics of the diagnostic methods that current psychiatric epidemiology (3, 5-7, Reich) now recognizes as essential: specific diagnostic criteria, use of best-estimate diagnosis, type of structured interview, family history, use of medical records, involvement of several diagnosticians, independence of diagnosticians, blindness of interviewer, blindness of final diagnosis to genetic marker, blindness to proband's diagnosis, blindness to family relationship, reliability checks, and uniformity of methods for all subjects.

First, most linkage studies of the last decade used the Research Diagnostic Criteria (RDC), and only recently have *DSM-III* criteria been used. The data suggest that the broader RDC diagnoses are 20% to 30% more inclusive than the narrower *DSM-III* criteria, at least for schizophrenia (55). There are also striking differences between reports in the use of a best-estimate method of diagnosis, blindness to proband's and relatives' diagnoses, the use of several independent diagnosticians, repetitive reliability checks, degree of certainty on diagnosis, and, most of all, inclusion of less definite or severe diagnoses in the first hierarchical (or certainty) level for entry in the linkage analysis. Table 1 shows that the Amish study by Egeland and associates (16) is one of the few studies that paid attention to almost all these methodological considerations.

Only 11 studies (15, 21, 25, 26, 28, 31, 40, 42, 44, 48, 54) (tables 1 and 2) used a consensus best-estimate procedure (6, 7), i.e., a final diagnosis that was based on a personal structured interview, all available medical records, and structured information from several family respondents and that was generated by several diagnosticians who were not themselves the interviewers and who had no contact with the field work and therefore could be blind to the proband's and relatives' diagnoses, as well as to the index marker. The majority of reports did not indicate whether the diagnosticians were blind. Other studies used only personal interviews or used a best estimate only when there was a disagreement between the two first interviewers, who were often not blind to the proband's diagnosis. Furthermore, only one group (Amish study [16]) assessed reliability of diagnosis at the best-estimate level in addition to the structured-interview level. Incidentally, only a few studies assessed interdiagnostician reliability at the interview level (14, 29). The vast majority of publications do not mention reliability of diagnosis at any level. This is worrisome, since linkage analyses are notoriously influenced by diagnostic misclassifications (1, 2, 4, 56).

Only 15 reports (8, 9, 12, 13, 15, 19, 24, 25, 32, 33, 40, 42, 50, 52, 54) refer to blindness to genetic marker, and only nine refer to blindness to the diagnosis of probands (28, 42, 54) or relatives (15, 25, 28, 40, 42, 44). In most pedigree studies, the diagnosticians or interviewers had contact in the field with the family members and perforce could not be blind to the proband's and relatives' clinical status in such densely affected families. Besides, in several studies diagnosticians who had no contact in the field were nevertheless aware that only one disease (either schizophrenia or bipolar disorder) was under study by their group, and the impact on final diagnosis of this knowledge is unknown.

Having more than one diagnostician generating the final diagnosis minimizes the risk of undue influence caused by the idiosyncrasies of the diagnostic opinions of any particular diagnostician (16). According to the reports on the 38 studies, only 17 used more than one diagnostician. In addition, to avoid the immediate influence of others in making a decision, it is advantageous for each diagnostician to first make an independent best-estimate diagnosis before coming to a consensus with two or three other diagnosticians. Only eight studies relied on such an independence (9, 11, 15, 18, 25, 40, 44, 54). In several studies, the investigators sought to establish a consensus immediately at the beginning of the process (52). In other studies, diagnoses were made by trained persons reviewing the written information taken from the interview and a consensus best estimate was used only in case of disagreement between the first diagnosticians (or interviewers), who often were unblind (9, 13, 19). In some of the studies shown in tables 1 and 2, a first investigator reviewed the diagnosis done in the field and then a second investigator did a final analysis of all the information (21, 22, 31, 42).

Several of the studies did not use the same diagnostic procedure for all subjects, and the possible artifact created by this difference has so far received little attention. The biggest problem in comparing the results, however, as shown in tables 1 and 2, is that the definition of the diagnostic first hierarchical (or certainty) level that was entered into the linkage analysis varies from one study to another. Very few reports included only the most severe diagnosis, either definitive schizophrenia (34, 37-40, 47, 52, 54) or bipolar disorder (15, 26, 33), in hierarchical level 1. In most studies, schizoaffective or unipolar disorders were entered into level 1. The inclusion of a broader spectrum of disorders in level 1 raises the risk of introducing more heterogeneity.

PRESENT STUDY

The present 59 subjects were members of several large multiplex families that are densely affected by schizophrenia or bipolar disorder (57). The subjects were from different socioeconomic backgrounds, they were between 18 and 89 years old (mean=50.6 years, SD=17.7), and 25 (42%) were male. These pedigrees

TABLE 1. Review of Diagnostic Procedures in Linkage Studies of Bipolar Disorder

Authors	Chromosomes and Index Markers ^a	Linkage ^b	Diagnostic Criteria	Type of Interview	Blindness of Interviewer ^c	Family History Data	Medical Records	Best-Estimate Procedure
Weitkamp et al. (8), 1980	6 (HLA), 28 other markers	No	Feighner, <i>DSM-III</i>	— ^f	— ^f	Yes, for unavailable first-degree relatives	— ^f	— ^f
Mendlewicz et al. (9), 1980	X (G6PD deficiency)	Yes	Feighner	CAPIES	Yes to genetic marker	— ^f	Yes	Only in case of disagreement between the two interviewers
Johnson et al. (10), 1981	1, 4, 6, 7, 9, 13, 16, 19 (HLA blood groups, serum proteins, red cell enzymes)	No	Feighner	Semistructured interview (not specified)	— ^f	— ^f	Yes	— ^f
Crowe et al. (11), 1981	30 markers	No	Feighner	Structured interview (not specified) by a psychiatrist	Not to relatives' and proband's diagnoses; one interviewer did all the interviews	— ^f	— ^f	No; final diagnosis based only on interview
Kruger et al. (12), 1982	5 (HLA)	Yes	<i>DSM-III</i>	SADS-L	Yes to index marker	Yes	Yes	— ^f
Goldin et al. (13), 1982	5 (HLA)	No	RDC	SADS rated by two independent investigators	Yes to index marker	Yes	Yes	Only in case of disagreement between the two raters; percentage not reported
Kidd et al. (15), 1984, described by Hostetter et al. (16), 1983	6 (HLA, GLC, BF)	No	RDC	SADS-L	No to family history and proband status	Yes, SADS (at least for one respondent)	Yes	Yes
Campbell et al. (17), 1984	6 (HLA)	No	RDC, FH-RDC for unavailable relatives	SADS-L reviewed blindly by psychiatrist	— ^f	FH-RDC for uninterviewed relatives	— ^f	— ^f
Del Zompo et al. (18), 1984	X (proton deaf-teran color blindness, G6PD deficiency)	Yes (lod score=1.47)	RDC	SADS rated by two independent psychiatrists	Yes to genetic marker	— ^f	— ^f	— ^f
Mendlewicz et al. (19), 1987	X (F9, locus)	Yes	RDC	Two independent SADS	Yes to proband's diagnosis and genetic marker	— ^f	Yes	Only in case of disagreement between the two investigators

Number of Diagnosis- ticians	Independence of Diagnosticians ^d	Final Diagnosis Blind to			Reliability of Diagnosis	Same Procedure for All Subjects	Diagnostic Hierarchy Levels ^e
		Genetic Marker	Proband's Diagnosis	Family Relation- ship			
— ^f	— ^f	Yes	— ^f	No	— ^f	— ^f	1) UP + undiagnosed psychiatric illness + SA
2 or 3	The two interview diagnoses were independent; independence for subjects receiving diagnoses from interview only, not applicable for best estimate	Yes	— ^f	Yes for best estimate; no for others	— ^f	No; best estimate only in case of disagreement between interviewers	1) BP + UP
— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	1) BP + UP
3	Yes in first step; consensus afterward	— ^f	— ^f	— ^f	— ^f	— ^f	1) UP, 2) level 1 + suspected UP, 3) UP + BP, 4) level 1 + alcohol/ drug abuse, 5) level 1 + undiagnosed psychiatric illness, 6) level 2 + BP, 7) levels 2 + 5, 8) all except undiagnosed
— ^f	— ^f	Yes	— ^f	— ^f	— ^f	— ^f	1) BP + UP, *2) level 1 + cyclothymia + dysthymia + borderline + labile + obsessive-compul- sive PD + schizotypal PD with depressive compo- nent + childhood psychosis
1		Yes	— ^f	— ^f	No reliability test on best estimate; reliability tests on interviews (Ma- zure et al. [14])	No; best estimate only in case of diagnostic disagreements	1) UP + BP1 + BP2 + SA
4	Yes in first step; consensus afterward	Yes	— ^f	Yes	Yes; concordance between a) Endi- cott and board, b) abstracted and integral records, c) SADS and best estimate	Yes; some diag- noses based on only records and family history, but concordance between methods was good	1) BP (definitive or probable), 2) level 1 + definitive or probable UP + other probable affective dis- orders, 3) level 2 + possible UP or BP + minor affective disorders
1		— ^f	— ^f	— ^f	— ^f	Yes since uninter- viewed subjects were not included	1) UP + BP + mania + hypomania + SA + minor depression
2	Yes	— ^f	— ^f	— ^f	— ^f	— ^f	1) BP + UP
2 or 3	Yes for subjects receiving diag- nosis from inter- view only; not applicable for best estimate	Yes	— ^f	Yes for best- estimate diagnosis; not re- ported for others	— ^f	No; best estimate only in case of disagreement be- tween two first investigators	1) BP + UP + cyclothymia

TABLE 1 (continued)

Authors	Chromosomes and Index Markers ^a	Linkage ^b	Diagnostic Criteria	Type of Interview	Blindness of Interviewer ^c	Family History Data	Medical Records	Best-Estimate Procedure
Hodgkinson et al. (20), 1987	11 (HRAS1, INS, TH)	No	RDC	SADS-L interview-diagnosis confirmed by two other psychiatrists	— ^f	— ^f	Yes	— ^f
Detera-Wadleigh et al. (21, 22), 1987, described by Gershon et al. (23), 1982	(21): 11 (HRAS1 and INS); (22): 3, 7 (somatostatin neuro-peptide Y)	No	RDC	SADS-L rated by two independent blind investigators; 26% done by phone	75% blind to family relationship	Yes	Yes	Yes; diagnosis made on records by two independent investigators
Baron et al. (24), 1987	X (color blindness and G6PD deficiency)	Yes	RDC	SADS for 90%; 5% by phone	Yes to genetic marker	Yes; FH-RDC	Yes	No; diagnosis made by clinical interviewer
Egeland et al. (25), 1987; Kelsøe et al. (26), 1989, described by Hostetter et al. (16), 1983	11 (INS, HRAS)	(25): yes; (26): no	RDC	SADS-L	No to family history and proband status	SADS (at least for one respondent)	Yes	Yes
Gill et al. (27), 1988	11 (HRAS, INS)	No	RDC	SADS-L	— ^f	— ^f	Yes	— ^f
Cox et al. (28), 1989; Andreasen et al. (29), 1981	18 markers	No	RDC	SADS 38% by phone	Yes to proband status	FH-RDC	Yes	Yes
Neiswanger et al. (30), 1990	11 (HRAS1, INS), X (DXS52)	No	RDC for adults; DSM-III-R for subjects under 18	SADS for adults; KIDIE SADS for subjects under 18	— ^f	Yes	— ^f	— ^f
Berrettini et al. (31), 1990	X (DXS215, DXS52, F8C)	No	Modified RDC	SADS rated by two independent blind investigators; 26% by phone	75% blind to family relationship	Yes	Yes	Yes; diagnosis made on records by two independent investigators
Baron et al. (32), 1990	X (color blindness and G6PD deficiency)	Yes	RDC	SADS for 90%; 5% by phone	Yes to genetic marker	Yes	Yes	No; diagnosis made by clinical interviewer
Holmes et al. (33), 1991	11 (P2 receptor, D11597, D11585, D11536, DRD2)	No	RDC	SADS-L	Yes to genetic marker	— ^f	Yes	— ^f

^aThe number refers to the chromosome on which the marker is located; the marker is in parentheses.

^bPresence of linkage defined as lod score greater than 3.

^cWhether or not the interviewer was blind to the genetic marker and/or proband's diagnosis and/or relatives' diagnoses.

^dWhether or not each diagnostician expressed an independent opinion before trying to reach a consensus with other diagnosticians.

Number of Diagnosticians	Independence of Diagnosticians ^d	Final Diagnosis Blind to			Reliability of Diagnosis	Same Procedure for All Subjects	Diagnostic Hierarchy Levels ^e
		Genetic Marker	Proband's Diagnosis	Family Relation- ship			
3	— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	1) BP + UP
2 for final best esti- mate	No; one reviewed all data on diag- nosis made by field team, then other confirmed diagnosis	— ^f	— ^f	— ^f	No reliability test on best-estimate diagnosis; reli- ability tests on interviews (Mazure et al. [14])	— ^f	1) BP1 + BP2 + SA + UP + anorexia
1		Yes	— ^f	— ^f	Reported as good; no details	No; 10% of unin- terviewed sub- jects were diag- nosed by family history only	*1) BP1 + BP2 + mania + UP + SA (mainly affective cyclothymic), *2) level 1 without cyclothymia
4	Yes in first step; consensus afterward	Yes	— ^f	Yes	Yes; concordance between a) Endi- cott and board, b) abstracted and integral records, c) SADS and best estimate	Yes; some diag- noses based on only records and family history, but concordance between methods was excellent	(26): 1) BP1 + BP2, 2) level 1 + UPR, 3) level 2 + UP, 4) level 3 + minor depres- sion; (25): 1) BP1 + BP2 + SA manic + UP + atypical psychosis
— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	1) UP + BP
1		— ^f	Yes	Yes	No reliability test on best estimate; reliability tests on interviews	Yes	Bipolar probands: 1) BP1 + SA, 2) level 1 + BP2, 3) level 1 + UP; unipolar probands: 1) UP
— ^f	— ^f	— ^f	— ^f	— ^f	Concordance of family history and SADS assessed in 42 subjects; 92% of family history diagnoses con- firmed by SADS	No; 43 of 64 subjects interviewed, diagnosis for others only from family history	1) UPR, 2) SA + BP1 + UP, 3) SA + BP1 + BP2 + UP + minor depression + cyclothymia + dysthymia
2 for final best esti- mate	No; one reviewed all data on diag- nosis made by field team, then other confirmed diagnosis	— ^f	— ^f	— ^f	No reliability test on best-estimate diagnosis; reliabi- lity tests on inter- views (Mazure et al. [14])	— ^f	1) BP1 + BP2 (with UP) + SA, 2) level 1 + UP, 3) cyclothymia + BP2 (with minor depression) + suicide + hypomania + eating disorders + SZ
1		Yes	— ^f	— ^f	Reported as good; no details	No; 10% of subjects uninterviewed, diagnosed by family history only	*1) BP1 + BP2 + mania + UP + SA (affective) + cyclothymia, *2) level 1 + BP2 + unipolar SA depressive, *3) BP + mania + SA manic, *4) level 1 + hypomania, *5) level 1 + minor depres- sion
1		Yes	— ^f	— ^f	— ^f	— ^f	1) BP1 + BP2, 2) level 1 + UP + minor depression + intermittent depression

^aBP=bipolar disorder; BP1=bipolar disorder, type 1; BP2=bipolar disorder, type 2; PD=personality disorder; SA=schizoaffective disorder; SZ=schizophrenia; UP=unipolar depression; UPR=unipolar depression, recurrent episodes. An asterisk marks the hierarchical level in which linkage was present.

^fNot reported.

TABLE 2. Review of Diagnostic Procedures in Linkage Studies of Schizophrenia

Authors	Chromosomes and Index Markers ^a	Linkage ^b	Diagnostic Criteria	Type of Interview	Blindness of Interviewer ^c	Family History Data	Medical Records	Best-Estimate Procedure
McGuffin et al. (34), 1983	1, 2, 4, 6, 7, 8, 9, 13, 14, 16, 19 (HLA, red cell antigens, plasma proteins, red cell enzymes)	No	CATEGO	PSE, border-line schedule	— ^f	— ^f	Yes	— ^f
Chadda et al. (35), 1986	6 (HLA)	No	RDC	— ^f	— ^f	— ^f	— ^f	— ^f
Goldin et al. (37), 1987	6 (HLA)	No	RDC	SADS-L, SIPD	— ^f	Yes	Yes	— ^f
Andrew et al. (38), 1987	1, 2, 4, 6, 7, 8, 9, 13, 14, 16, 19 (HLA, red cell antigens, plasma proteins, red cell enzymes)	No	PSE, ICD-9, DSM-III	PSE	— ^f	— ^f	Yes	— ^f
Kennedy et al. (39), 1988	5 (D5S21, D5S76, D5S39, D5S78, HEX-B, CRL, D5S22, DHFB)	No	RDC, Feighner for schizophrenia; not reported for others	SADS-L	No to relatives' and proband's diagnoses; one psychiatrist interviewed all patients	— ^f	Yes	No
Sherrington et al. (40), 1988	5 (D5S39, D5S76)	Yes	RDC, DSM-III	SADS-L for 98 of 134; six were briefly screened	No to relatives' and proband's diagnoses; yes to genetic marker	— ^f	Yes	Yes
St-Clair et al. (41), 1988	11 (HRAS1, IHS)	No	RDC	Yes	— ^f	— ^f	Yes	— ^f
Detera-Wadleigh et al. (42), 1989, described by Gershon et al. (43), 1988	5 (D5S39, D5S76, DHFR)	No	RDC	SADS-L, SIPD	Yes to relatives' diagnoses; 2/3 blind to proband's diagnosis	Yes	Yes	Yes
Kaufmann et al. (44), 1989	5 (D5S21, D5S76, D5S5, D5S39, D5S78)	No	DSM-III-R, RDC	SADS-L	No to relatives' and proband's diagnoses	Yes	Yes	Yes
St-Clair et al. (45), 1989	5 (D5S39, D5S76, D5S78)	No	RDC	SADS-L	— ^f	— ^f	Yes	No; final diagnoses by the three psychiatrists who did the interviews
Diehl and Kendler (46), 1989	5	No	— ^f	— ^f	— ^f	— ^f	— ^f	— ^f
Aschauer et al. (47), 1990	5 (D5S20, D5S76, D5S39, DHFR)	No	DSM-III-R	DIS, structured psychiatrist interview	— ^f	Yes	Yes	— ^f
DeLisi et al. (48), 1991, described in DeLisi et al. (49), 1987	Xq27, Xq28 (DXS105, DXS374, DXS52, F8C)	No	RDC (modified)	Modified SADS-L for U.S. sample, in person or by phone; PSE for U.K. sample	Yes to family status	Yes	Yes	Yes (U.S. sample)

Number of Diagnosis- ticians	Independence of Diagnosticians ^d	Final Diagnosis Blind to			Reliability of Diagnosis	Same Procedure for All Subjects	Diagnostic Hierarchy Levels ^e
		Genetic Marker	Proband's Diagnosis	Family Relation- ship			
— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	1) SZ, 2) level 1 + paranoid psychosis + positive on borderline schedule
— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	1) SZ and SZ spectrum dis- order of Kety et al. (36)
— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	1) chronic SZ + indeterminant SZ, 2) level 1 + schizotypal PD + paranoid PD
— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	A) 1) PSE broad description of SZ, 2) level 1 + schizotypal and paranoid PD; B) ICD-9; C) DSM-III
1		— ^f	No	No	— ^f	Yes	1) SZ
2	Yes	Yes	— ^f	Yes	— ^f	Yes	*1) SZ, *2) level 1 + schizoid + schizotypal PD, *3) level 2 + any psychiatric disorder
— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	1) SZ + other psychoses
2	No; one reviewed all data on diag- nosis made by field team, then other confirmed diagnosis	Yes	Yes	Yes	— ^f	— ^f	1) SZ + SA, 2) level 1 + schizotypal + schizoid + paranoid PD, 3) level 2 + UP + BP
2	Yes	— ^f	— ^f	Yes	— ^f	Yes	1) SZ + SA
3	— ^f	— ^f	No	No	— ^f	Yes	1) SZ + SA + BP + psychosis (unspecified), 2) level 1 + UP, 3) level 2 + other RDC diagnoses
— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	— ^f
— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	1) SZ, 2) level 1 + schizotypal + SA, 3) level 2 + any psychi- atric diagnosis
2 (U.S. sample)	— ^f	— ^f	— ^f	Yes	Yes; values not reported	— ^f	1) SZ + SA, 2) level 1 + BP + UP + schizotypal PD

TABLE 2 (continued)

Authors	Chromosomes and Index Markers ^a	Linkage ^b	Diagnostic Criteria	Type of Interview	Blindness of Interviewer ^c	Family History Data	Medical Records	Best-Estimate Procedure
St-Clair et al. (50), 1990	Translocation 1:11	Yes	RDC	SADSL for 30 of 52 subjects	No to relatives' and probands' diagnoses; same two interviewers did all interviews	Yes	Yes	— ^f
McGuffin et al. (51), 1990	5 (D5S39, D5S76, D5S78)	No	DSM-III-R	PSE; checklist for schizotypic symptoms	— ^f	— ^f	Yes; scored on OPCRIT	— ^f
Crowe et al. (52), 1991	5 (D5S39, D5S21, D5S76, D5S78, D5S76)	No	DSM-III-R	CASH (53), SSP	— ^f	Yes	Yes	— ^f
Maziade et al. (54), in press	Balanced 2:18 translocation	No	DSM-III-R	SCID	Yes to genetic marker	Yes	Yes	Yes

^aThe number refers to the chromosome on which the marker is located; the marker is in parentheses.

^bPresence of linkage defined as lod score greater than 3.

^cWhether or not the interviewer was blind to the genetic marker and/or proband's diagnosis and/or relatives' diagnoses.

^dWhether or not each diagnostician expressed an independent opinion before trying to reach a consensus with other diagnosticians.

were selected in eastern Quebec in the framework of our program of genetic epidemiology and molecular genetics of major psychoses. We integrated in the study design repetitive reliability assessments at different levels of the diagnostic procedure. We report here on one aspect of reliability: the concordance between two independent consensus best-estimate diagnoses, one blind and the other unblind to the diagnoses of probands and relatives, to prior clinicians' diagnoses, and to response to treatment.

Best-Estimate Method

We designed our field procedure, our blind best estimate by a psychiatric panel, and our reliability tests while considering the 13 methodological points mentioned previously.

Field procedure. The first home visit is performed by a research psychiatrist or a senior professional assistant, who explains the study and obtains consent. Through subsequent home visits, trained and clinically experienced professional interviewers administer the Structured Clinical Interview for DSM-III-R (SCID) (58) to which have been added a few modules of the Comprehensive Assessment of Symptoms and History (CASH) (53), especially those on the negative and positive symptoms of schizophrenia. This interview is audiotaped and the interviewers are blind to genetic markers, as are all the personnel working in the field. In addition, for each subject, at least two family respondents are interviewed through a structured family history interview composed of a list of 14 items. When an

item is rated positively, it refers to a checklist of symptoms corresponding to a *DSM-III-R* diagnosis (7). All available medical records are reviewed and edited to remove 1) identification of the subject, the treating physician, and the hospital, 2) past and current diagnoses by the clinicians, and 3) type of treatment and response to treatment. The last two are abstracted separately.

Then, under the supervision of the research psychiatrists in the field, the professional assistant highlights all the clinical information from the medical records that is pertinent to diagnosis and summarizes it, summarizes the personal interview and family history, and, still under the supervision of the field research psychiatrists (M.M., C.C., M.-A.R.), writes out a differential diagnosis while noting the presence or absence of each pertinent symptom and diagnostic criterion according to *DSM-III-R*, the RDC, and a clinical impression outside current classifications. After all possible information has been gathered, a consensus diagnosis (including a degree of certainty) for each episode and a consensus lifetime diagnosis are made by the field psychiatrists (M.M., C.C., M.-A.R.).

Blind psychiatric board procedure. A panel of four experienced and trained psychiatrists is kept blind to genetic markers, the proband's diagnosis (schizophrenia or bipolar disorder) and family relationships, prior clinicians' diagnoses, and response to treatment. The board is fed a complete diagnostic record consisting of edited raw clinical information—i.e., the audiotape (edited to keep the board blind) of the SCID interview in addition to the SCID ratings and notes made by the interviewer—photocopies of the edited original medical

Number of Diagnos- ticians	Independence of Diagnosticians ^d	Final Diagnosis Blind to			Reliability of Diagnosis	Same Procedure for All Subjects	Diagnostic Hierarchy Levels ^e
		Genetic Marker	Proband's Diagnosis	Family Relation- ship			
— ^f	— ^f	Yes	— ^f	— ^f	— ^f	No; 30 of 58 diagnosed with interviews, others with fami- ly history, rec- ords, discussion with clinicians	1) SA + SZ, 2) level 1 + UPR, 3) level 2 + adolescent conduct and emotional disorders, 4) and 5) level 3 + GAD + UP + alcoholism
— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	— ^f	1) SZ + schizophreniform disorder + delusional disorder + UP with mood- incongruent delusions
2	No; immediate consensus was reached	Yes	— ^f	— ^f	— ^f	— ^f	1) SZ, 2) level 1 + SA + schizo- phreniform disorder + schizotypal PD, 3) level 2 + any axis I DSM-III-R diagnosis
4	Yes	Yes	Yes	Yes	Yes	Yes	1) SZ

^aBP=bipolar disorder; GAD=generalized anxiety disorder; PD=personality disorder; SA=schizoaffective disorder; SZ=schizophrenia; UP=unipo-
lar depression; UPR=unipolar depression, recurrent episodes. An asterisk marks the hierarchical level in which linkage was present.

^fNot reported.

record notes, and data from structured interviews of family respondents (family history). Psychiatrist 1 reviews all this material, including the SCID audiotape, while psychiatrist 2 independently reviews all of this information except the audiotape. Separately they each make *DSM-III-R*, RDC, and clinical impression diagnoses. Then they discuss the case.

In case of complete agreement between psychiatrists 1 and 2, the complete diagnostic board record is presented at a board meeting and each symptom or diagnostic criterion (*DSM-III-R*, RDC) is reviewed systematically by the four psychiatrists, voted on, and rated before a final consensus diagnosis (with a certainty level) is rendered. The president of the board summarizes the discussion while emphasizing whatever areas of difficulty there were in reaching a consensus.

In case of a disagreement between psychiatrists 1 and 2, the SCID audiotape is sent to psychiatrist 2 and the complete diagnostic board record is forwarded to psychiatrists 3 and 4 before the board meeting. Again, each states an independent diagnostic opinion before the board meeting, during which the process previously described is then conducted.

Reliability Results

Table 3 presents the level of concordance between the consensus best-estimate diagnosis made in the field by two psychiatrists of the research team (M.M. or C.C. or M.-A.R.) with their experienced field interviewers and the one made blindly and independently by the board of four psychiatrists. When we used very strin-

gent criteria, i.e., also considered as a disagreement a discordance of one or two points on the certainty scale (1, definite diagnosis; 2, probable; 3, possible) for the same diagnosis, then a concordance rate of 78% was obtained for the whole sample ($\kappa=0.83$) and 71% ($\kappa=0.76$) was obtained for the 45 subjects who were given *DSM-III-R* diagnoses in the field. When only a difference in *DSM-III-R* diagnosis was considered as a disagreement, the concordance rose to 90% ($\kappa=0.88$) in the whole sample and 87% ($\kappa=0.83$) in the clinical sample. This is very satisfactory if compared to the reliability of the best-estimate procedure found in the study by Leckman et al. (6) ($\kappa=0.45-0.84$), in the Amish study (16) ($\kappa=0.68-0.95$), and in others (59) ($\kappa=0.63-0.82$).

All of the subjects who were found definitely normal by the diagnosticians in the field were also judged as such by the psychiatric board. Among the 45 subjects given *DSM-III-R* diagnoses according to the best estimate in the field, the board of psychiatrists arrived at a different conclusion for 13 subjects. However, for seven of these 13 subjects, the disagreements involved only the degree of certainty (definite, probable, possible) for the same diagnosis rather than a difference in *DSM-III-R* diagnosis. We found a statistically significant tendency of the field best estimates toward greater certainty levels and toward more consistency with the most prevalent disorder of the pedigree (either schizophrenia or bipolar disorder); this was true for 10 of the 13 total cases of disagreement (binomial exact test of $H_0=50\%$, $p<0.05$) and for all of the six disagreements on diagnosis (binomial exact test, $p<0.01$).

TABLE 3. Concordance Between Unblind Best-Estimate Diagnoses in the Field and Diagnoses Made by a Panel of Four Blind Psychiatrists for Subjects From Families Censely Affected by Schizophrenia or Bipolar Disorder

Sample and DSM-III-R Category	Cases of Disagreement		Cases of Agreement		Kappa	
	Total	Disagreement or Certainty ^a	Diagnosis Present	Diagnosis Absent	Disagreements on Diagnosis Only	Disagreements on Certainty Included ^b
Whole sample (N=59)	13	7	32	14	0.88	0.83
Subjects who received field diagnoses (N=45)	13	7	32		0.83	0.76
Affective spectrum	9	7	16	20	0.90	0.81
Bipolar I	5	3	10	30	0.85	0.80
Bipolar II	0		3	42	1.00	
Major depression					0.92	0.84
Single episode	2	2	2	41		
Recurrent	2	2	1	42		
Schizophrenic spectrum	4	0	10	31	0.71	0.74
Schizophrenia	1	0	10	34	0.77	0.77
Schizoaffective disorder	3	0	0	42	-0.03	-0.02
Alcohol dependence	0		3	42	1.00	
Other diagnoses	0		3	42	1.00	
Adaptation disorder	0		1	44	1.00	
Generalized anxiety disorder	0		1	44	1.00	
Delusional disorder	0		1	44	1.00	

^aOne- or two-point discordance on the certainty scale (1, definite=2, probable; 3, possible) on the same diagnosis, rather than disagreement on type of diagnosis.

^bKappa also considers as a partial disagreement a one- or two-point discordance on the certainty scale (1, definite; 2, probable; 3, possible) on the same diagnosis; weight given to difference on certainty scale: absolute difference of 0, weight=1; difference of 1, weight=2/3; difference of 2, weight=1/3; difference of 3, weight=0.

In addition to the seven disagreements on the certainty level of the same diagnosis, the differences in DSM-III-R diagnoses were the following. In the bipolar pedigrees, one schizoaffective depressive disorder (probable) diagnosed by the unblind team was diagnosed as a schizophreniform disorder (definite) by the panel, another schizoaffective depressive disorder (probable) was diagnosed by the board as schizophrenia (definite), one bipolar disorder (definite) was rediagnosed as schizoaffective disorder, and another bipolar disorder (definite) was rediagnosed as schizophrenia (probable). In the schizophrenia pedigrees, the one case of schizophrenia (definite) diagnosed by the unblind team was diagnosed by the board as organic mental syndrome (probable), and a schizoaffective disorder (probable) was rediagnosed as a bipolar disorder (definite). The concordance on severity of diagnosis, as determined by the Global Assessment Scale scores (60), was also satisfactory (intraclass correlation=0.82).

DISCUSSION

False positive or unreliable diagnoses might have a disastrous effect on the results of genetic linkage analysis of schizophrenia and bipolar disorder (1-4, 15, Reich). Our review of prior genetic linkage studies of schizophrenia and bipolar disorder shows serious discrepancies between studies in diagnostic methods. Paying attention to the 13 methodological points derived from this review should minimize diagnostic biases and improve the comparability of studies. In our present study we found a high reliability level with a consensus best estimate based on these 13 features.

However, whereas the presently observed concordance between an unblind best estimate made in the field and that made by a board of four blind psychiatrists could be considered as very satisfactory for other epidemiological purposes, it can have a strong impact on results of linkage studies, even more so because our results show that the unblind consensus best estimates made by the field team were biased toward a higher level of certainty or severity of diagnoses in the schizophrenia or bipolar spectrum and were also biased toward more consistency with the most prevalent diagnosis (either schizophrenia or bipolar disorder) in the respective multiplex pedigrees. In other words, unblind diagnosticians tended, for instance, to diagnose more affective disorders in bipolar pedigrees than the blind psychiatric board did. This finding is noteworthy if one considers that very few prior articles on linkage (see tables 1 and 2) reported complete diagnostician blindness to the proband's and relatives' diagnoses and that most groups were studying only one disorder (schizophrenia or bipolar) at a time, implying that the diagnosticians were aware of the familial disorder under investigation. Of course, the question of the exact origin of this field bias remains: Does it come from knowing in advance about the most prevalent disorder in the selected pedigrees, from being aware of the subjects' past diagnoses noted in the medical records by clinicians, or from knowledge of the subjects' response to treatment (i.e., neuroleptics versus antidepressants versus lithium)?

Schizoaffective diagnosis appears less reliable in the Amish study (16), where three of the seven diagnoses of schizoaffective disorder led to disagreements on the best-estimate diagnosis (kappa=0.71). So far, we have found disagreements for the three schizoaffective cases

in our sample. Similarly, Strober et al. (59) found a lower kappa (0.63) for schizoaffective disorders. However, in a large number of linkage studies (see tables 1 and 2) schizoaffective disorder was inserted in the first hierarchical level for analysis. The impact of this inclusion on results is unknown.

Our results call for further reliability studies of different aspects of the consensus best-estimate diagnosis in our sample and in others—for instance, the effect of editing material on the response to treatment, the concordance between diagnoses based on different sources of information, and the identification of the type of clinical cases that lead more often to disagreements on diagnosis. Our results also support our present, time-consuming effort to feed the board of blind psychiatrists with the edited raw clinical information from the interviews and medical records, instead of providing solely clinical material that has been sifted and abstracted by field interviewers or trained research assistants. The latter inevitably cannot be blind to the proband's and relatives' status while working with such densely affected pedigrees. Providing the board with raw clinical information and arranging to study simultaneously pedigrees affected by bipolar disorder and others affected by schizophrenia ultimately constitute the only way of keeping a board of diagnosticians really blind to the most prevalent disorder of these large multiplex pedigrees.

In conclusion, as clarified in recent meetings on psychiatric genetics (3, 4, Reich), any new genetic linkage study of major psychoses must include 1) the use of multiple diagnostic classifications because of the uncertain validity of any one set of criteria, 2) the use of several levels of certainty or severity in the diagnostic hierarchy, 3) the gathering of extensive clinical information, 4) a best-estimate procedure of diagnosis based on multiple sources of information, 5) blindness to the diagnoses of the proband and relatives, 6) follow-ups to establish stability of diagnoses.

To this list we suggest adding 1) the participation in the best-estimate procedure of two or more blind diagnosticians who are not at all involved in the data gathering, 2) an independent opinion by each blind diagnostician before a consensus with the others is reached, 3) repetitive reliability checks at the best-estimate level rather than only at the structured-interview level, since most of the time diagnosis is far from being based only on this latter source of information, 4) forwarding of edited raw clinical information to the blind panel of diagnosticians, rather than information already filtered, abstracted, or interpreted by unblind field investigators, and 5) simultaneous investigation by the board of blind diagnosticians of at least two different familial disorders (for instance, schizophrenia and bipolar disorder) so that the diagnosticians will be really blind to the proband's and relatives' diagnoses.

Most of all, our review again indicates that it is imperative that researchers enter only the most severe or definite diagnosis in the first hierarchical level for linkage analysis (1, 3, 4, Reich) and that publications pro-

vide a minimal description of the diagnostic procedure according to current standards in order to permit replication (61). Several of the most recent reports do not even provide this information. Finally, our results call for further studies of the impact and origin of this field bias on diagnosis in pedigree studies.

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Combined Pharmacotherapy and Psychotherapy in the Acute and Continuation Treatment of Elderly Patients With Recurrent Major Depression: A Preliminary Report

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***Objective:** The authors examined the rate of response to the combination of nortriptyline and interpersonal psychotherapy for acute and continuation treatment of elderly patients with recurrent major depression. **Method:** The subjects were 73 elderly patients, 61 of whom completed treatment. Nortriptyline steady-state blood levels were maintained at 80–120 ng/ml, and interpersonal psychotherapy was administered weekly for 9.1 weeks (median) of acute therapy and was decreased from biweekly to triweekly during 16 weeks of continuation therapy. During acute treatment nonresponding patients also received brief adjunctive pharmacotherapy with lithium or perphenazine. **Results:** Of the 61 subjects given adequate trials of nortriptyline and interpersonal psychotherapy, 48 (78.7%) achieved full remission (Hamilton depression rating of 10 or lower over 16 weeks of continuation therapy), 10 patients (16.4%) did not respond (Hamilton rating never below 15), and three achieved only partial remission (Hamilton rating of 11–14). Early versus late onset was not associated with a difference in response rate. During the placebo-controlled, double-blind transition to maintenance therapy, 19 (76.0%) of the 25 patients randomly assigned to placebo maintenance conditions showed continued recovery and six relapsed. None of the 24 patients assigned to nortriptyline conditions relapsed. **Conclusions:** Use of nortriptyline plus interpersonal psychotherapy for 9.1 weeks (median) of acute and 16 weeks of continuation therapy appears to be associated with good response and relatively low attrition but about a 25% chance of relapse during double-blind discontinuation of nortriptyline. These data require confirmation in a controlled clinical trial of acute and continuation therapy.*

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The 1991 National Institutes of Health (NIH) Consensus Development Conference on the Diagnosis and Treatment of Depression in Late Life (1) highlighted the need for clinical trials assessing the efficacy

of combination pharmacotherapy and psychotherapy in the acute, continuation, and maintenance treatment of elderly patients with major depression, particularly those with recurrent illness. The published data are based on trials assessing the efficacy of a single intervention—either drug alone or psychotherapy alone but not both. Treatment success rates have been around 50%–70% in both drug (2, 3) and psychotherapy (4, 5) controlled trials enrolling older subjects with major depression, but many of these subjects were not truly elderly and most were outpatients. Also, most of these studies were relatively brief trials (generally 7 weeks or less) of acute therapy and the reports contain little information about the stability of therapeutic response during continuation therapy or about continued remission after drug discontinuation (6).

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Because of the need for information regarding the efficacy of combined therapy both acutely and during continuation therapy, we report here the first 2 years of experience in the University of Pittsburgh's Maintenance Therapies in Late-Life Depression study. The primary objective of the study is to assess the efficacy of maintenance nortriptyline and interpersonal psychotherapy (7) singly and in combination, under randomized, double-blind, placebo-controlled conditions, with respect to maintenance of recovery over a 3-year period after open-trial acute and continuation treatment of the index episode. Treatment of the index episode involves combined therapy with both nortriptyline and interpersonal psychotherapy under open-trial conditions. The investigators' choice of combination therapy for the non-experimental acute and continuation phases of the protocol (reported here) reflects the expectation that such an approach is likely to maximize the number of patients available for the subsequent experimental maintenance phase of the protocol. It also reduces the probability of bias on the part of patients and clinicians as to which treatment is likely to be most efficacious in the maintenance of recovery. It was required that a patient achieve remission and remain well for 16 weeks of continuation therapy (with both modalities) before random assignment to one of four maintenance therapies (medication clinic with placebo, medication clinic with nortriptyline, interpersonal psychotherapy plus placebo, and interpersonal psychotherapy plus nortriptyline). The investigators initially projected that 65% of the patients entering the protocol would meet the criteria for randomization, after remission of the index episode.

We provide in this report preliminary data on treatment success and stability of response, treatment failure, and attrition during combination acute and continuation therapy. We also report the rates of relapse during transition to maintenance treatment, where one-half of the patients are randomly assigned to placebo conditions under double-blind discontinuation conditions. We emphasize that the study is ongoing, with intake now at the halfway point, and that the data reported here are from an open trial complemented by placebo-controlled, double-blind discontinuation of nortriptyline. In light of the need for information about combination therapy identified by the 1991 NIH consensus conference (1), however, we believe that the results are sufficiently promising and instructive to warrant preliminary communication.

METHOD

Subjects

During the first 24 months of the study, 73 patients 60–80 years old (mean=67.5, SD=5.8) entered the protocol. The female/male ratio was 53/20; seven (9.6%) of the subjects were black, and 66 (90.4%) were white. The marital status distribution was as follows: widowed, N=29 (39.7%); married, N=27 (37.0%); divorced,

N=9 (12.3%); never married, N=5 (6.8%); remarried, N=1 (1.4%). The mean education level was 11.8 years (SD=2.4).

Approximately 48% of the subjects responded to media announcements, and 52% were referred through traditional medical channels. Approximately 243 subjects were screened in face-to-face interviews to yield the current group of 73 (a 30% yield). The patients were required to be experiencing at least the second lifetime episode of major depression (nonbipolar, non-delusional), to have a score on the 17-item Hamilton Rating Scale for Depression (8) of at least 17 after 14 days without psychotropic drugs, and to have had an interepisode wellness interval of at least 2 months but no longer than 2.5 years. Diagnoses were made by using the Schedule for Affective Disorders and Schizophrenia—Lifetime Version (SADS-L) (9) in an interview conducted by trained master's level psychiatric nurses and were confirmed in an independent interview by a senior faculty psychiatrist. Fourteen patients (19.2%) were diagnosed as having nonendogenous depression, 16 (21.9%) had probable diagnoses of endogenous depression, and 43 (58.9%) had definite diagnoses of endogenous depression. Twenty (27.4%) of the 73 patients reported that the first episode of major depression had occurred at age 60 or later ("late onset"), and 53 (72.6%) reported an earlier onset; the mean age at first episode was 47.5 years (SD=17.0). A review of past SADS-L diagnoses (definite) indicated the following rates: hypomania, 1.4% (N=1); panic disorder, 2.7% (N=2); generalized anxiety disorder, 5.5% (N=4); Briquet's disorder, 2.7% (N=2); alcoholism, 4.1% (N=3); drug use disorder, 1.4% (N=1); and phobic disorder, 2.7% (N=2). No patients met the criteria for cyclothymic personality, labile personality, antisocial personality, obsessive-compulsive disorder, or any psychotic disorders.

Forty-two percent of the patients (N=31) had major psychosocial problems requiring social service intervention. Twenty-five percent (N=18) required inpatient hospitalization during the acute therapy of the index episode, and 11.0% (N=8) had histories of suicide attempts. The median number of prior episodes of major depression was three. Upon entry into the protocol the 73 patients had a mean Hamilton depression rating of 22.3 (SD=3.8), a Beck Depression Inventory (10) score of 24.2 (SD=9.9), and a Global Assessment Scale (GAS) (11) score of 55.7 (SD=5.2). The mean duration of the index episode was 39.9 weeks (SD=35.8).

Almost all patients entering the protocol were under concurrent medical surveillance for chronic but stable (nonprogressive) medical disorders that did not contraindicate nortriptyline or require medications known to cause depression. Review of current medical status indicated the following frequencies of medical problems: cardiac, 41.1% (N=30); musculoskeletal, 39.7% (N=29); osteoarthritis, 30.1% (N=22); lower gastrointestinal, 32.9% (N=24); diverticulitis, 9.6% (N=7); upper gastrointestinal, 24.7% (N=18); fatal hernia, 17.8% (N=13); genitourinary, 39.7% (N=29); benign prostatic hypertrophy, 11.0% (N=8); vascular, 32.9% (N=24); hypertension, 20.5% (N=15); eyes, ears, nose,

and throat, 30.1% (N=22; cataracts, 12.3%; glaucoma, 5.5%); endocrine, 21.9% (N=16; thyroid, 9.6%; diabetes mellitus, 6.8%); neurologic (e.g., laminectomy, neurofibromatosis, and carpal tunnel syndrome), 13.7% (N=10); pulmonary, 15.1% (N=11; chronic obstructive pulmonary disease, 5.5%). Similarly, review of concurrent nonpsychotropic medications indicated the following rates of use: anti-inflammatory, 19.2% (N=14); endocrine, 13.7% (N=10); calcium channel blockers, 12.3% (N=9); diuretics, 15.1% (N=11); hormone replacements, 5.5% (N=4); β blockers, 6.8% (N=5); H_2 blockers, 5.5% (N=4); eye medications, 4.1% (N=3); theophylline, 1.4% (N=1).

Procedure

For the patients beginning treatment on an outpatient basis, acute therapy of the index episode consisted of combination nortriptyline and interpersonal psychotherapy, with weekly visits to the outpatient research clinic. Nortriptyline was prescribed by faculty psychiatrists in doses sufficient to produce a steady-state blood level of 80–120 ng/ml. The patients were instructed to take the full daily dose of nortriptyline at bedtime, and blood samples for determination of nortriptyline levels were taken 12–16 hours later. The blood levels were monitored weekly during acute therapy and biweekly to triweekly during continuation therapy. Interpersonal psychotherapy was delivered during weekly 50-minute sessions by experienced psychotherapists trained to, and maintained at, research levels of proficiency in interpersonal psychotherapy. All therapy sessions were audiotaped, and a random sample of 20% were rated for interpersonal psychotherapy specificity. Procedures for adapting interpersonal psychotherapy to use with elderly patients have been incorporated into a manual written by several of us (E.F., C.C., S.D.I., M.D.M., and C.F.R.).

A brief course of adjunctive pharmacotherapy (4–6 weeks), i.e., lithium (0.6–1.0 meq/liter), perphenazine (4–12 mg/day), or both, was permitted if the patient had not achieved full response after 8 consecutive weeks of nortriptyline at a therapeutic steady-state level (80–120 ng/ml). After a Hamilton rating of 10 or lower was achieved, adjunctive medication was discontinued. Unless the patient maintained a Hamilton rating of 10 or lower while receiving nortriptyline (alone) plus interpersonal psychotherapy, he or she could not enter continuation therapy.

A patient entered continuation therapy after meeting two criteria: 1) a Hamilton depression rating of 10 or lower for 3 consecutive weeks and 2) a steady-state nortriptyline blood level of at least 50 ng/ml. The purpose of continuation therapy was to ensure stability of response for 16 consecutive weeks before random assignment to a maintenance therapy cell. The frequency of clinic visits decreased to every other week for the first 8 weeks of continuation therapy and then to every third week during the final 8 weeks, in anticipation of monthly visits during the 3-year experimental maintenance phase of the study.

At the end of continuation therapy, the patient was randomly assigned to one of the four maintenance treatments; there was a 50% chance of being assigned to a nortriptyline cell and a 50% chance of being assigned to a placebo condition. During the 4–6-week transition to maintenance treatment, the nortriptyline dose of the patients assigned to placebo was gradually tapered by 20%–25% weekly under double-blind conditions.

Analysis

The major outcome measure, treatment success, was defined as remission of depressive symptoms (Hamilton depression rating of 10 or lower) sustained over 16 weeks of continuation therapy, as required for random assignment to a maintenance therapy cell. Our choice of a Hamilton score of 10 or lower as indicative of remission in the elderly is consistent with the findings of Georgotas et al. (12). However, we also examined outcome by using the more stringent criterion of a mean Hamilton depression rating of 6 or less during the final two ratings (over 4 weeks) at the end of continuation therapy.

RESULTS

Attrition

Of the 73 patients enrolled, 12 (16.4%) were removed from the study during screening or acute therapy. The reasons for attrition were treatment refusal or noncompliance (N=8), intercurrent medical conditions contraindicating further use of nortriptyline (N=3), and spontaneous remission during the 2-week psychotropic-drug-free observation period before the start of acute therapy (N=1). Two additional patients were lost during continuation: one died of a myocardial infarction, and one left the study against medical advice. Thus, a total of 59 patients (80.8% of those entering the study) completed the acute and continuation trial of combination nortriptyline and interpersonal psychotherapy (at least 26 weeks of acute therapy in the case of nonresponders).

Treatment Response

Sixty-one patients (83.6% of those entering) completed acute treatment and were therefore considered to have had adequate trials. Of the 61 completers, 48 (78.7%) responded fully; an additional three patients had partial responses (Hamilton scores of 11–14). Ten of the 61 patients who completed acute treatment were nonresponders (Hamilton depression ratings of 15 or higher) after at least 26 weeks of acute treatment (mean=35.8, SD=19.4), representing a treatment failure rate of 16.4%. Thus, 65.7% of those who entered and 78.7% of those who had adequate exposures to treatment could be considered treatment responders according to a criterion of a Hamilton score of 10 or less. Ac-

TABLE 1. Treatment Characteristics and Depression Scores for Elderly Depressed Patients Who Did or Did Not Respond to Combined Nortriptyline and Interpersonal Psychotherapy

Group and Time	Time From Intake (weeks)		Nortriptyline Dose (mg/day)		Nortriptyline Blood Level (ng/ml)		Hamilton Depression Score ^a	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Full and partial responders (N=51)								
Treatment start	2.3	1.6					18.9	4.4
First response	13.3	8.0	80.7	30.7	88.6	27.0	6.7	2.8
Remission	33.6	12.4	83.1	35.0	88.7	28.5	5.0	3.2
Nonresponders (N=10)								
Treatment start	2.3	1.2					22.5	4.1
Declaration of failure	35.8	19.4	63.0	32.3	95.7	29.0	19.7	5.3

^a17-item Hamilton Rating Scale for Depression.

cording to the more stringent criterion of a Hamilton score of 6 or less, 56.2% of those who entered and 67.2% of those who received adequate trials would be considered responders (N=41).

Age at first episode (≤ 60 or ≥ 60 years) was not specifically associated with rate of treatment success. Of the 20 late-onset patients, 14 (70.0%) responded fully, and of the 53 early-onset patients, 34 (64.2%) responded fully.

Among the 51 patients with full or partial responses were five patients (9.8%) who relapsed during continuation therapy (Hamilton depression rating of 17 or above) but were successfully restabilized for the 15-week period of symptomatic remission required for random assignment to a maintenance therapy cell. The 10 nonresponders included four patients who showed brief symptomatic remission but subsequently relapsed and could not be restabilized.

Of the 25 patients assigned to placebo maintenance conditions, six (24.0%) relapsed during double-blind discontinuation of nortriptyline. Three had been assigned to placebo plus maintenance interpersonal psychotherapy, and three had been assigned to placebo plus medication clinic. None of the patients assigned to continuation of full-dose nortriptyline (N=24) suffered a relapse during the double-blind 4–6-week transition to maintenance therapy (Fisher's exact test, $p=0.02$).

The nortriptyline doses and blood levels and the Hamilton depression scores before and during treatment are shown in table 1. The Hamilton scores showed a mean drop of 71.0% (SD=12.2%) in the full and partial responders versus 9.2% (SD=29.7%) in the nonresponders.

Treatment Variables

The median duration of acute treatment for the 51 patients who completed treatment was 9.1 weeks (range=2.7–37.3). For the group of full and partial responders the mean duration of acute treatment was 11.2 weeks (SD=7.8), and the median was 10.0 weeks (8.6 weeks for the full responders and 26.6 weeks for the partial responders). These calculations do not take into account the additional time needed to restabilize

the five patients who relapsed during continuation therapy.) An examination of cumulative response time indicated that 44 (72.1%) of the treatment completers (86.3% of the 51 total responders) entered the continuation phase by 17 weeks. The nortriptyline doses and steady-state blood levels are shown in table 1.

During acute therapy, 17 (33.3%) of the total responders received brief courses (4–6 weeks) of adjunctive lithium carbonate (0.6–1.0 meq/liter) or perphenazine (4–12 mg/day). Inpatients were more likely to receive augmentation therapy: 13 of 18 (72.2%). Remission had to be sustained, however, after discontinuation of adjunctive medication for a minimum of 3 weeks before the patient was entered into the continuation treatment phase of the protocol. Adjunctive lithium or perphenazine was not allowed during continuation therapy.

DISCUSSION

The rate of full response in this study (65.7% of enrolled patients and 78.7% of completers) obtained with a combination of pharmacotherapy and psychotherapy is encouraging, since the study group consisted of elderly patients with highly recurrent major depression and moderate to severe impairment. Furthermore, the observation that 67.2% of the treatment completers had Hamilton scores of 6 or less by the end of continuation therapy suggests that the majority of the successfully treated patients had few residual depressive symptoms, a problem frequently noted in clinical trials for late-life depression. Such a finding also suggests that lower expectations for the quality of response in the elderly may not be justified. The overall attrition rate (16.4%) compares favorably to rates of 24%–42% typically reported in geriatric clinical trials (2, 3, and unpublished 1991 report by L.W. Thompson and D. Gallagher-Thompson), and the low failure rate (16.4%) also compares favorably to rates reported in the literature (33%–40%).

Furthermore, we used a conservative definition of treatment success, one requiring stability of response (remission) for 16 consecutive weeks of continuation

therapy. Without such a requirement, the true clinical significance of "treatment success" is diminished. The mean reduction in Hamilton depression ratings, 71.0%, is also clinically meaningful. This concept is further supported by increases in GAS scores from 55.7 (SD=5.2) at study entry to 76.6 (SD=5.8) at the start of continuation therapy and to 82.3 (SD=5.5) at the end of continuation therapy.

The use of a double-blind, placebo-controlled design for the transition to maintenance therapy permits a further assessment of the stability of recovery. With a 4–6 week transition to maintenance and a 20%–25% reduction of nortriptyline dose weekly and concurrent introduction of placebo, 19 (76.0%) of 25 patients randomly assigned to placebo showed no evidence of relapse. The 24.0% relapse rate among the placebo patients (versus 0% relapse among the nortriptyline patients) suggests several possibilities: 1) the brittle nature of the response of some geriatric patients; 2) the possible need for a longer period of continuation therapy; 3) the need for a longer period for drug discontinuation, with a slower rate of drug withdrawal; and/or 4) a discontinuation effect of interpersonal psychotherapy in some patients.

These results, while promising, are based on the open-trial, uncontrolled phase of the larger study. By design, control groups (monotherapy with placebo, nortriptyline, or interpersonal psychotherapy) are not used during this phase, the purpose of which is to maximize the number of remitted patients available for the experimental maintenance phase (which uses random assignment, placebo control, and double-blind procedure). Hence, the current results must be viewed as preliminary, and generalization to clinical practice can be made only with caution. Furthermore, both phases of the protocol (open acute/continuation, controlled maintenance therapy) are being carried out in a treatment-intensive research clinic where patients are monitored very closely. The magnitude of nonspecific effects is difficult to estimate in the absence of a placebo control during the acute/continuation phase. Finally, it should be borne in mind that the study group consists of "young old" patients (60–80-year-olds) who are living in the community and have little functional impairment in activities of daily living, not medically frail "old old" who are institutionalized (13).

In a review of 25 double-blind antidepressant drug studies published between 1964 and 1986 that focused on patients over 55 years of age, Gerson et al. (2) concluded that "drugs are clearly superior to placebo; they show comparable therapeutic efficacy—about 50% improvement in Hamilton Psychiatric Rating Scale for Depression scores versus 20% to 25% on placebo." In perhaps the most rigorous study to date, Georgotas et al. (12) reported a rate of response (Hamilton rating of 10 or lower) of 60% for both nortriptyline and phenelzine versus a 13% response rate for placebo among depressed patients 55 years of age and older who were treated for 7 weeks. Georgotas et al. (14) also reported additional benefit from extending the antidepressant

medication trial past 7 weeks to 9 weeks. Addition of this 2-week period was associated with an increase in the response rate to 69%. A caveat would appear to be appropriate in interpreting these data on extending duration of therapy: if a trial goes on long enough, some patients may improve spontaneously.

The most extensive research experience with the psychotherapy of late-life depression was reported by Thompson et al. (4). These investigators reported a study of 91 elderly outpatients with a major depressive disorder (more than 50% with recurrent major depression) who were treated with 16 to 20 sessions of behavioral, cognitive, or brief psychodynamic psychotherapy. The authors used a 6-week delayed-treatment control condition and reported a 24% dropout rate overall. The major finding of the study was that "by the end of six weeks patients in the [active] treatment conditions showed improvement, whereas controls did not. Overall, 52% of the treatment sample attained remission by termination; another 18% showed significant improvement."

These studies using drug alone or psychotherapy alone for elderly outpatients with major, unipolar, non-delusional depression resulted in treatment success rates of 60%–70% at 6–9 weeks, versus 0%–13% for wait-list/control or placebo conditions. Our current experience of using combination nortriptyline and interpersonal psychotherapy has yielded a somewhat higher success rate (78.7% for the completers) and a dropout rate of only 16.4%, over an acute treatment period lasting a median of 9.1 weeks in all completers (range=2.7–37.3 weeks), in a somewhat older and medically more complicated population. Although this comparison might be viewed as evidence of the superiority of combined pharmacotherapy and psychotherapy, it is probably confounded by different durations of acute therapy (7–9 weeks for Georgotas et al. [12, 14], 6 weeks for Thompson et al. [4], and 2.7–37.3 weeks in the current study), the use of adjunctive medication in the current study, and possible differences in referral biases, portals of entry, subject inclusion/exclusion criteria, and definitions of outcome. More recently, Thompson and Gallagher-Thompson have reported an improvement rate of over 90% in elderly depressed outpatients (mean age=66.7 years) treated with combination desipramine and cognitive-behavior therapy over 6–10 months (unpublished 1991 report). In that study, "improvement" meant a reduction of symptoms great enough that the patient no longer qualified for a Research Diagnostic Criteria diagnosis of major depressive disorder. This success rate appears similar to ours (78.7%), except that their definition of "improvement" may have allowed greater residual symptoms.

Prospective, controlled clinical trials will be necessary to demonstrate the superiority of combination therapy over monotherapy in the acute/continuation treatment of major depression in elderly patients. Such a trial is indicated by comparison of the current preliminary results with published data from controlled trials assessing monotherapeutic interventions. In addition to their

possible clinical utility, such trials would possess clinical face validity by mimicking actual clinical practice and might illumine the possible synergy frequently hypothesized for combination therapy. The low dropout rate observed (16.4%) may partly account for the encouraging preliminary outcome here.

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Religious Coping and Depression Among Elderly, Hospitalized Medically Ill Men

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Objective: The investigators examined the frequency of religious coping among older medical inpatients, the characteristics of those who use it, and the relation between this behavior and depression. **Method:** The subjects were 850 men aged 65 years and over, without psychiatric diagnoses, who were consecutively admitted to the medical or neurological services of a southern Veterans Administration medical center. Religious coping was assessed with a three-item index. Depressive symptoms were assessed by self-rating (the Geriatric Depression Scale) and observer rating (the Hamilton Rating Scale for Depression). **Results:** One out of every five patients reported that religious thought and/or activity was the most important strategy used to cope with illness. Variables that were associated with religious coping included black race, older age, being retired, religious affiliation, high level of social support, infrequent alcohol use, a prior history of psychiatric problems, and higher cognitive functioning. Depressive symptoms were inversely related to religious coping, an association which persisted after other sociodemographic and health correlates were controlled. When 202 men were reevaluated during their subsequent hospital admissions an average of 6 months later, religious coping was the only baseline variable that predicted lower depression scores at follow-up. **Conclusions:** These findings suggest that religious coping is a common behavior that is inversely related to depression in hospitalized elderly men.

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Medical illness that precipitates hospitalization is a stressful experience that can interrupt social and work routines, drain finances, separate families, reverse caregiver roles, and create situations of forced dependency. Physical illness also brings with it the threat of pain and long-term disability, disfigurement, the prospect of approaching death, and feelings of existential anxiety and sometimes despair. During physical illness coping resources are seriously tested and frequently overwhelmed, as evidenced by the fact that 40% or more of older hospitalized patients experience some form of clinical depression (1, 2). Religious beliefs and behavior, in turn, are prevalent among older persons (3,

4) and are reported to serve as a coping strategy to help manage emotional distress (5-8). The extent to which older medical inpatients use religion for this purpose, the characteristics of those who do so, and the effectiveness of this strategy are largely unknown.

National samples of Americans of all ages indicate that persons who find personal comfort and support from religion are more likely to be older, female, black, less educated, widowed, employed in manual or unskilled occupations, more economically deprived, and affiliated with conservative Protestant religious denominations (3). These sociological findings suggest that persons with fewer health, social, and financial resources, when facing situations over which they have little control (such as acute hospitalization), might turn to religion for solace.

Whether religious beliefs and behavior actually help to prevent or relieve emotional distress is far from clear. Psychiatric illness may be even more common among the religious (9-11), perhaps predisposing them to greater problems in later life when they are faced with the stress of physical illness and/or approaching death. Thus far, systematic research on the relation between religious coping and depression among older adults in

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clinical settings has been limited. Previous studies have been hampered by small sample sizes, less than rigorous sampling methods, and unequal sex distribution (few males) (6-8).

This report emanates from the Durham Veterans Administration (VA) Mental Health Survey (12, 13), a cross-sectional and longitudinal epidemiologic study of depression among hospitalized medically ill men. We examine religious coping, its sociodemographic and health correlates, and its relation to depression both cross-sectionally and over time. Four major questions guided this investigation: 1) How common is religious coping in this population? 2) Is this coping behavior more likely among those with fewer socioeconomic, physical, or mental health resources? 3) When other factors are controlled, is there an association between religious coping and depression? 4) If such a relationship exists, is it especially strong in any subgroup of the population, such as those with more severe medical illness, low social support, prior mental health problems, or other attributes?

METHOD

Between Sept. 1, 1987, and Jan. 1, 1989, all men aged 65 years and over who had been admitted to medical or neurological services at the Durham VA Medical Center were screened for depression. For inclusion in the study, patients were required to score 15 or higher on the Mini-Mental State examination (14) and to be physically capable of undergoing a psychiatric evaluation. Psychiatric patients were excluded. Patients were evaluated within 48-72 hours of admission by a social worker and/or a Fellow in geriatric medicine (H.G.K.).

Data were collected on demographic characteristics and social and economic resources, including age, race, education, prior occupation (15), retirement status, current living situation, marital status, yearly income, and social support. Social support was measured with a three-item index that explored size of the support network (16), frequency of interaction, and perceived adequacy of support (17) (values for each item ranged from 1 to 5; Cronbach's $\alpha=0.57$). Over 40 religious denominations were represented in the study group; these were categorized into nine general religious groups according to a schema provided by Rof and McKinney (18).

The physical health of the participants, including medical diagnoses, functional status, and cognitive status, was assessed. Functional status was determined by measuring physical (19) and instrumental (20) activities of daily living. Physical activities of daily living included bathing, dressing, toileting, problems with incontinence, transfer from bed to chair or vice versa, and feeding (each rated 0-2); instrumental activities of daily living involved ability to travel, shop, prepare meals, do housework, and handle finances (rated 0 or 1). These two types of ratings together produced an 11-item scale with a possible range of scores from 0 (low functioning)

to 17 (high functioning). As we have mentioned, cognitive status was measured with Mini-Mental State examination scores, which ranged from 15 to 30.

The assessment of mental health included information on alcohol use, prior psychiatric problems, and family history of psychiatric problems. Depression was assessed by self-rated and observer-rated scales. The self-rated 30-item Geriatric Depression Scale (21) was administered by the social worker to all patients; this scale has been validated as a measure of depression in older medical inpatients (22). The men aged 70 years and older were also assessed by one of us (H.G.K.) with the Hamilton Rating Scale for Depression (23), a measure used in other studies of the elderly (24) and medical inpatients (25). Depression scales were administered early in the interview, before the assessment of religious coping.

Religious coping was assessed with a three-item index. Each item measured how much the patient relied upon religion to help manage the emotional stress associated with his illness. In item 1, the patient was asked an open-ended question about how he coped. This item was chosen in order to identify the coping behavior that the patient himself felt was most helpful, and the question was asked before questions on religion that might bias responses. If the response was religious in nature (e.g., faith in God or Jesus, prayer, church), the patient received a score of 10; if the spontaneous response was not religious (e.g., stay busy, family support), a score of 0 was assigned. A value of 10 for religious responses was chosen in order to give this item equal weight with the others in the index.

In item 2, patients were asked to rate on a visual analog scale the extent to which they found religious beliefs or activities helpful in coping with their situation. The scale was numbered from 0 ("not much or not at all") to 10 ("the most important thing that keeps me going"). In approaching patients with the rating scale, the investigators allowed patients to define for themselves the meaning of the term "religion" but made clear that this could involve personal belief alone or include religious activity such as prayer or church attendance.

In item 3, the interviewer rated the patient on a scale of 0-10 on the basis of an overall assessment of how much the patient used religion to cope. This judgment was based on the patient's further elaboration on religious coping themes during answers to items 1 and 2 and on a separate discussion about how religion was helpful. The scores from the three items were then summed, and an index with values ranging from 0 to 30 was obtained. Cronbach's α (reliability) for the index in the overall sample ($N=850$) was acceptable (0.82).

Test-retest/interrater reliability for the religious coping index was also determined for a subgroup of 188 consecutively admitted men. The religious coping index was administered twice to these patients, each time by a different rater; ratings were separated by 12-36 hours. The Pearson correlation between scores obtained on the religious coping index at the two administrations was 0.81. The interrater agreement for the ob-

server-rated religious coping item (item 3) was surprisingly high (Pearson's $r=0.87$) given that the raters came from markedly different religious backgrounds (secular humanist versus conservative Protestant).

All participants in the baseline study who were readmitted to the medical or neurological services during the 16-month study period and 5 months thereafter (designated "time 2") were reevaluated by the social worker with the Geriatric Depression Scale and the religious coping index. Again, psychiatric admissions were excluded. If more than one readmission occurred, the results from the last interview during the 21-month observation period was used for time 2. This provided information on change in depressive symptoms and religious coping over time among patients whose medical illness prompted rehospitalization during the project.

Analyses were performed with the SAS statistical package (26). Simple statistics were used to determine the frequency of spontaneously reported, self-rated, and observer-rated religious coping. Bivariate relations of covariates with religious coping (religious coping index score) and depression (Geriatric Depression Scale and Hamilton depression scale scores) were examined with Pearson correlations. Hierarchical regression was used to examine the strength of relationships, controlling for the effects of other covariates.

To determine whether patients who used religious coping had fewer socioeconomic or health resources than other patients, the religious coping index score was regressed on a series of 16 demographic, socioeconomic, and health variables (excluding depression). A backward stepwise regression method was used to eliminate nonsignificant variables ($p>0.05$); missing values were dealt with by listwise deletion. The regression was performed in five stages. In the first stage, demographic variables (age, race, and occupational and retirement status) were entered into the model. In subsequent stages, religious affiliation, socioeconomic resources, and mental and physical health variables were added. The fifth stage produced a final model that contained the significant correlates.

We examined the relation between depression and religious coping in the following manner. First, a model for depressive symptoms was constructed by regressing it on the 15 sociodemographic and health variables (excluding religious variables). Once a final model had been obtained, we added religious coping and religious affiliation variables. Interactions between religious coping and all other variables in the model were tested and included in the final model if alpha was less than or equal to 0.05. Regression models were developed for both self-rated symptoms (Geriatric Depression Scale) and observer-rated symptoms (Hamilton Rating Scale for Depression).

We analyzed the longitudinal data as follows. Pearson correlations determined bivariate relations between baseline (time 1) group characteristics and follow-up (time 2) Geriatric Depression Scale score. Hierarchical regression was then used to assess the relation between time 1 religious coping index score and time 2 Geriatric Depression

TABLE 1. Sociodemographic and Health Characteristics of 850 Elderly Male Medical Inpatients

Characteristic	Mean	SD	N	%
Demographic				
Age (years)	69.8	4.9		
Black race			240	28.3
Education (years)	8.9	3.8		
Unskilled occupation			333	39.2
Retired more than 5 years			589	69.3
Social/economic				
Married			577	67.9
Living alone			160	18.8
Income (dollars per year)	8,582	3,316		
Social support rating ^a	10.6	1.8		
Mental health				
History of psychiatric problems			216	25.7
Family history of psychiatric problems			76	9.1
Alcohol use			153	18.2
Geriatric Depression Scale score ≥ 11			186	22.1
Hamilton depression score ≥ 15			49	14.7
Physical health				
Medical diagnosis				
Cancer			188	22.1
Gastrointestinal disease			125	14.7
Neurological disease			122	14.4
Respiratory disease			87	10.2
Renal disease			40	4.7
Cardiovascular disease			216	25.4
Other			72	8.5
Functional status (activities of daily living) ^b	14.1	4.0		
Cognitive status (Mini-Mental State score) ^c	26.4	2.8		

^aRange of possible scores=3–15.

^bRange of possible scores=0–17.

^cRange of possible scores=0–30.

Scale score, controlling for time 1 Geriatric Depression Scale score and other significant baseline correlates.

RESULTS

There were 1,110 consecutively admitted new patients during the study period. Eight hundred fifty men (77%) underwent comprehensive social, psychological, and physical health examinations; 260 did not participate because of advanced dementia or delirium (12% with Mini-Mental State scores less than 15), communication problems (2%), refusal or discharge before being seen (5%), or other reasons (4%). Nonparticipants were more likely to be older, black, and residents of nursing homes and to have diagnoses of neurological or respiratory illness.

The sociodemographic and health characteristics of the subjects are presented in table 1. The distributions of race, marital status, and medical diagnoses were similar to those among elderly male patients discharged from VA hospitals in District 8, which covers most of North Carolina and parts of Virginia, Kentucky, Tennessee, and South Carolina (12). Table 2 presents the

TABLE 2. Distribution of Religious Affiliations Among 850 Elderly Male Medical Inpatients, Elderly Men in Central North Carolina, and in the United States as a Whole

Religious Group ^c	Percent of Elderly Male Medical Inpatients	Percent of Elderly Men in Central North Carolina ^b	Percent in U.S. Population ^a
Liberal Protestant (Episcopal, United Church of Christ, Presbyterian)	8.0	7.1	8.7
Moderate Protestant (Methodist, Lutheran, Disciples of Christ, Reformed)	12.5	17.2	19.3
Conservative Protestant (White Baptist, Church of Christ, Nazarene, Seventh-Day Adventist)	40.8	54.7 ^c	11.3
Black Protestant (Methodist, Baptist)	22.2		5.3
Fundamentalist/evangelical (Pentecostal, Holiness, Assemblies of God, Church of God)	5.1	5.1	4.7
Protestant (unspecified)	3.3	5.9	
Catholic	2.6	1.5	25.3
Jewish	0.0	0.3	2.3
Nontraditional Christian (Mormon, Jehovah's Witnesses, Christian Science, Unitarian)	3.2	3.3	8.3
No religious preference	2.4	5.1	6.3

^aSee Roof and McKinney (18).^bMen aged 55 years and over who participated in the Piedmont Epidemiological Catchment Area study (central North Carolina) (27).^cIncludes conservative Protestants and black Protestants.

religious affiliations of the participants. The distribution was comparable to that of elderly men living in central North Carolina; compared to the population of the nation as a whole, however, a disproportionate number of men came from conservative or black Protestant denominations (63% in this study, 54% in central North Carolina, and 17% nationally).

In response to the open-ended question directed at how they coped, 20% (N=167) of the subjects (24% of those aged 70 years and over) spontaneously replied that religion was a primary factor. Religion in this sense typically involved having trust or faith in God, praying, reading the Bible or other religious literature, listening to religious programs on the radio or watching religious programs on television, participating in church services or other related activity, and receiving emotional support from church members or a pastor. On the visual analog scale, which ranged from 0 to 10, the mean rating by patients was 6.5 (SD=3.1). More than half of the subjects (56%, N=471) rated themselves 7.5 or higher, and 21% gave themselves a rating of 10 (religion being "the most important thing that keeps me going"). Observer ratings of religious coping for the group ranged from 0 to 10, with a mean 5.7 (SD=3.2). The religious coping index scores for the group ranged from 0 to 30; the mean was 14.3 (SD=8.7).

TABLE 3. Bivariate Relation of Covariates to Religious Coping and Depression (Pearson correlations) Among 850 Elderly Male Medical Inpatients

Covariate	Religious Coping ^a (N=842)	Depression ^b	
		Geriatric Depression Scale (N=841)	Hamilton Depression Scale (N=333)
Demographic characteristics			
Age	0.05	-0.02	-0.02
Race	0.15 ^c	-0.09 ^d	-0.04
Education	-0.00	-0.09 ^d	-0.11 ^e
Occupation	0.00	0.06	0.05
Retirement status	0.08 ^c	-0.11 ^d	-0.02
Social/economic resources			
Living situation	-0.01	0.03	0.03
Marital status	0.06	-0.10 ^d	-0.10
Income	0.05	-0.09 ^d	-0.13 ^e
Social support	0.12 ^c	-0.24 ^c	-0.21 ^c
Mental health			
History of psychiatric problems	0.03	0.30 ^c	0.27 ^c
Family history of psychiatric problems	0.08 ^e	0.13 ^c	0.11 ^e
Alcohol use	-0.16 ^c	-0.08 ^e	-0.15 ^c
Physical health			
Functional status (activities of daily living)	0.01	-0.26 ^c	-0.17 ^d
Cognitive status	0.05	-0.19 ^c	-0.11 ^e
Medical diagnosis			
Cancer	-0.01	-0.00	-0.01
Gastrointestinal disease	0.02	0.01	0.02
Neurological disease	-0.02	-0.03	-0.01
Respiratory disease	-0.03	0.16 ^c	0.14 ^d
Renal disease	0.03	0.02	-0.02
Cardiac disease	0.04	-0.08 ^e	0.00
Miscellaneous	-0.02	-0.03	-0.12 ^e
Religious affiliation			
Liberal Protestant	-0.07 ^e	-0.00	0.07
Moderate Protestant	-0.06	-0.06	-0.12 ^e
Conservative Protestant	-0.02	0.11 ^c	0.02
Black Protestant	0.12 ^c	-0.10 ^d	-0.04
Fundamentalist/evangelical	0.17 ^c	0.00	0.07
Protestant (unspecified)	-0.05	0.04	-0.10
Catholic	-0.11 ^d	-0.06	0.09
Nontraditional Christian	0.04	-0.01	-0.07
No religious preference	-0.15 ^c	0.06	0.14 ^d

^aMeasured with the religious coping index.^bScores on the Hamilton depression scale were available only for men aged 70 years and over. For categorical variables, point biserial correlations are reported. The correlation between Geriatric Depression Scale and Hamilton depression scale scores was 0.66.^cp≤0.001.^dp≤0.01.^ep≤0.05.

Sociodemographic and Health Correlates of Religious Coping

The bivariate relations of covariates to religious coping are presented in table 3 (column 1). Race, retirement status, social support, family history of psychiatric problems, and alcohol use were significant correlates. Liberal Protestants, Catholics, and patients with no affiliation were less likely to use religious coping (negative correlations), whereas black Protestants and members of fundamentalist/evangelical groups were more

TABLE 4. Religious Coping Regressed on Sociodemographic and Health Variables for 850 Elderly Male Medical Inpatients^a

Variable	Beta ^b
Demographic characteristics	
Age	0.12 ^c
Race	0.20 ^c
Retirement status	0.07 ^d
Religious affiliation ^e	
Liberal Protestant	0.20 ^f
Moderate Protestant	0.27 ^c
Conservative Protestant	0.49 ^c
Black Protestant	0.38 ^c
Fundamentalist/evangelical	0.37 ^c
Protestant (unspecified)	0.12 ^d
Catholic	0.05
Nontraditional Christian	0.21 ^c
Social support	0.12 ^c
Mental health	
History of psychiatric problems	0.07 ^d
Alcohol use	-0.14 ^c
Cognitive status	0.10 ^f

^aRegression analysis was performed in five stages; this table represents the fifth and final model (model $F=9.5$, $df=15$, 810, $p\leq 0.001$; total $R^2=0.15$).

^bBetas are standardized; for every 1 standard deviation change in the independent variable there is a beta standard deviation change in religious coping, with all other variables in the model controlled.

^c $p\leq 0.001$.

^d $p\leq 0.05$.

^eDummy variables were created to represent each religious group and were then compared to variables for patients with no religious affiliation (partial $F=7.8$, $df=8$, 828, $p\leq 0.001$).

^f $p\leq 0.01$.

likely to use religious coping than were members of other religious groups.

Using hierarchical stepwise regression, we examined the relations between religious coping and sociodemographic and health characteristics. In stage 1, age, race, education, and occupational status were entered as independent variables into a model with religious coping index score as the dependent variable. In stages 2 through 5, religious affiliation, social/economic resources, and mental and physical health variables were added successively to the model. At each stage, nonsignificant variables were excluded by using backward stepwise elimination. Variables unrelated to religious coping and thus dropped from the model were education and occupational status (stage 1), living situation, marital status, and income (stage 3), family history of psychiatric problems (stage 4), and functional status and medical diagnosis (stage 5). The fifth and final model is presented in table 4.

Religious affiliation accounted for the largest proportion of explained variance (46%). Men from conservative, black, and fundamentalist Protestant denominations were especially likely to use religion to cope. Demographic variables (age, race, and retirement status), social support, and mental health variables (history of psychiatric problems and use of alcohol) each accounted for about 15% of the explained variance in religious coping. Patients who were older, were black, had a history of psychiatric problems, and reported greater social support were more likely to use religion

as a coping behavior. Patients who used alcohol, on the other hand, were less likely to do so. The only physical health factor related to religious coping was cognitive status, which accounted for about 8% of the explained variance. Contrary to expectation, there was no significant relation between religious coping and functional status or medical diagnosis.

Religious Coping and Depression

Bivariate analyses indicated inverse correlations between religious coping index scores and both self-rated and observer-rated depression scores (Geriatric Depression Scale score, $r=-0.16$, $p\leq 0.001$; Hamilton depression score, $r=-0.14$, $p\leq 0.01$). We then used hierarchical regression to control for the confounding effects of other sociodemographic and health correlates of depression. Stepwise procedures were used to construct two models for depression (Geriatric Depression Scale scores and Hamilton depression scores as dependent variables). Fifteen sociodemographic and health variables (excluding religion) were examined as possible correlates of depression in each model.

In the development of the Geriatric Depression Scale model, variables unrelated to Geriatric Depression Scale score and thus eliminated were marital status, retirement status, occupational status, income, education, and living situation. Variables included in the final model were age, race, social support, history of psychiatric problems, family history of psychiatric problems, alcohol use, cognitive status, functional status, and six medical diagnoses (respiratory disease in particular [13]) (model $F=20.7$, $df=14$, 807, $p\leq 0.001$; $R^2=0.26$). Religious affiliations were then added but did not contribute significantly (partial $F=0.8$, $df=8$, 799, $p>0.50$). Finally, religious coping index score was added to the model, yielding a partial F of 19.8, $df=1$, 799, $p\leq 0.001$ (table 5, first column). The inverse relation between religious coping and depressive symptoms was stronger among men who had more severe disability (partial $F=3.9$, $df=1$, 798, $p\leq 0.05$). Religious coping index score did not interact significantly with any other correlates of depression, although the relation between religious coping index score and depression did tend to be stronger in men who had a prior history of psychiatric problems (partial $F=3.3$, $df=1$, 797, $p=0.07$).

We then examined the relation between religious coping index score and observer-rated depressive symptoms (in men aged 70 years and over). A model of significant correlates of Hamilton depression scale score was created (religious factors excluded). Variables related to Hamilton depression score and controlled for in the model were social support, history of psychiatric problems, alcohol use, and functional status (model $F=15.0$, $df=4$, 318, $p\leq 0.001$; $R^2=0.16$). The addition of religious affiliations contributed significantly to the model—largely a result of inverse associations between Hamilton depression scale score and moderate Protestant and Catholic affiliations. Finally, religious coping index score was added; it was inversely correlated with

TABLE 5. Self-Rated and Observer-Rated Depressive Symptoms Regressed on Religious Coping, With Other Correlates of Depression Controlled, for Elderly Male Medical Inpatients

Religious Variable	Beta ^a	
	Self-Rated Depressive Symptoms ^b	Observer-Rated Depressive Symptoms ^c
Religious coping index score	-0.14 ^d	-0.19 ^d
Religious coping index score by functional status	0.25 ^e	0.21
Religious affiliation ^f		
Liberal Protestant	n.s.	-0.06
Moderate Protestant	n.s.	-0.25 ^e
Conservative Protestant	n.s.	-0.23
Black Protestant	n.s.	-0.17
Fundamentalist/evangelical	n.s.	0.01
Protestant (unspecified)	n.s.	-0.00
Catholic	n.s.	-0.17 ^g
Nontraditional Christian	n.s.	-0.12 ^e

^aBetas are standardized; for every 1 standard deviation change in the independent variable (i.e., religious coping index score) there is a beta standard deviation change in Geriatric Depression Scale score or Hamilton depression score, with all other variables in the model controlled. For religious coping index score, SD=8.7; for Geriatric Depression Scale score, SD=5.3; for Hamilton depression scale score, SD=6.0.

^bGeriatric Depression Scale (model F=20.1, df=16, 798, p<0.001; total R²=0.29).

^cHamilton depression scale (only for men aged 70 years and over) (model F=7.4, df=13, 306, p<0.001; total R²=0.24).

^dp<0.001.

^ep<0.05.

^fReligious groups compared to patients with no religious affiliation (for religious affiliation in the Hamilton depression scale model, partial F=2.7, df=8, 310, p=0.01).

^gp<0.01.

Hamilton depression scale score (partial F=12.2, df=1, 306, p<0.001) (table 5, second column). There were no significant interactions between religious coping index score and other variables in the model.

Follow-Up Phase

In the follow-up phase, 256 (30%) of the 850 participants were readmitted to the hospital one or more times during the 16-month study and 5 months thereafter. Of these patients, 202 (79%) received complete follow-up evaluations, including both Geriatric Depression Scale and religious coping index assessments. The time from index hospitalization to readmission evaluation ranged from 0 to 20 months (mean=6 months). Compared with the 850 participants in the baseline study, readmitted patients were more likely to have a diagnosis of cancer (33% versus 22%) and less likely to have neurological disease (7% versus 14%); otherwise, they were similar in all other sociodemographic and health characteristics. The overall mean changes in both religious coping index score and Geriatric Depression Scale score (time 1 to time 2) were small (1 point or less). There was no relation between change in religious coping index score and change in depressive symptoms (Pearson's $r=0.06$, $p=0.45$).

Baseline predictors of time 2 Geriatric Depression Scale

TABLE 6. Follow-Up (Time 2) Geriatric Depression Scale Score Regressed on Baseline (Time 1) Religious Coping Index Score, With Other Baseline Predictors Controlled, for 202 Elderly Male Medical Inpatients

Variable ^a	Beta ^b
Time 1 Geriatric Depression Scale score	0.62 ^c
Medical diagnosis	
Cancer	-0.06
Gastrointestinal disease	-0.06
Neurological disease	-0.04
Respiratory disease	-0.08
Renal disease	0.15 ^c
Cardiovascular disease	-0.11
Time 1 religious coping index score	-0.18 ^e

^aFourteen baseline variables were not significantly related to time 2 Geriatric Depression Scale score and were dropped from the model. Dummy variables were created for each medical diagnosis; the missing category was other medical diagnoses. For medical diagnoses in the model: partial F=2.1, df=6, 196, p<0.05 (model F=20.0, df=8, 193, p<0.01; total R²=0.45).

^bBetas are standardized; for every 1 standard deviation change in the independent variable (e.g., time 1 religious coping index score), there is a beta standard deviation change in time 2 Geriatric Depression Scale score, with all other variables in the model controlled. For time 1 religious coping index score, SD=8.7; for time 2 Geriatric Depression Scale score, SD=5.8.

^cp<0.001.

^dp<0.05.

^ep<0.01.

score were then examined. Bivariate analyses demonstrated significant correlations between time 2 Geriatric Depression Scale score and time 1 Geriatric Depression Scale score ($r=0.64$), social support ($r=-0.16$), functional status ($r=-0.20$), diagnosis of renal disease ($r=0.15$), and time 1 religious coping index score ($r=-0.24$). To control for confounding, hierarchical stepwise regression was again used (table 6). Time 1 Geriatric Depression Scale score was entered first into the model, followed by 15 other predictors, with time 1 religious coping index score entered last. The final model contained three variables that predicted 45% of the variance in time 2 Geriatric Depression Scale score: time 1 Geriatric Depression Scale score, six medical diagnoses (renal disease in particular), and time 1 religious coping index score. No interactions between variables in the final model were significant. Thus, religious coping was the only baseline variable that predicted lower depression scores on follow-up (partial F=10.4, df=1, 193, $p=0.002$).

DISCUSSION

We found that religious beliefs and behavior were commonly used to manage stress in this medically ill group of older adults. When asked how they coped with their situations, 20% of the men spontaneously gave a response involving religion. Patients reported that trust or faith in God, prayer, Bible reading, and strong church relationships gave them comfort and a feeling of peace. We recognize that this finding may be in part due to the nature and location of our sample (southern VA

hospital). A relatively high proportion of these patients were affiliated with conservative or black Protestant groups, whose traditions place strong emphasis on religion as a source of comfort in times of stress. The high rate documented among this all-male study group, however, is notable because religious coping is generally more common among women than men (3, 28), suggesting that this behavior might be even more prevalent in hospital samples that include women.

What are the characteristics of men who use religion to cope? Do they experience greater stress than other patients? Do they possess fewer socioeconomic or physical or mental health resources? In general, this was a group of older patients who had relatively severe medical illnesses, often advanced functional disabilities, low educational levels (the majority with less than a high school education), and yearly incomes averaging less than \$10,000. The high rate of religious coping in this population, as we have discussed, suggests that it may indeed be characteristic of those with fewer coping resources. Within this group, however, there was no association between religious coping and level of functional disability, income, education, or previous occupation. On the other hand, religious coping was more common among those who were older, were black, or reported prior psychiatric problems—patients who may be more vulnerable to psychosocial or health stressors.

Furthermore, the strongest correlate of religious coping was religious affiliation (conservative, black, and fundamentalist/evangelical Protestant groups). This association by itself may have socioeconomic and health implications. The Piedmont Epidemiologic Catchment Area study showed that older members with these affiliations were more likely to come from lower socioeconomic classes, have lower educational levels, and have more chronic health problems and physical disabilities (27). Because these affiliations encourage affective release and emphasize religion as a source of comfort to those who are suffering, they may draw socioeconomically deprived or physically impaired elders into their congregations.

Some correlates of religious coping suggest mechanisms by which this behavior may help reduce stress and facilitate adaptation. Religious coping was positively related to both high level of social support and avoidance of alcohol, factors which in a VA hospital population could help to protect against emotional illness. Social support was one of the strongest inverse correlates of depression in these subjects (12). Religion may enhance social support by providing contacts with age-matched peers and/or by encouraging the development of supportive relationships within the religious community. In a study of older medical outpatients in Springfield, Ill., more than one-half of the subjects indicated that nearly all of their five closest friends came from their church congregations (4). For older black persons in particular, the church is reported to be a major source of informal social support (29).

Although many older men claimed that religion was helpful in coping with their illness, is there any evidence

to substantiate these reports? We found religious coping to be inversely related to depression, whether assessed by self-report (Geriatric Depression Scale) or by clinician rating (Hamilton Rating Scale for Depression). This relationship was stronger among men who were more functionally disabled, and tended to be so among patients who reported histories of psychiatric problems. Note that these were also the groups who were the most depressed. Other investigators have similarly found an inverse correlation between religious cognition/behavior and depression in physically ill elders (30, 31) and those with psychiatric illness (32, 33). Thus, these findings provide further evidence that religious coping behavior is especially helpful to older patients with few other physical or emotional resources. Studies have shown that when older persons are in situations over which they have little control, religious beliefs and behavior may counteract feelings of helplessness, provide meaning and order to experiences, and give back a sense of control (34, 35).

An alternative explanation for the inverse relation between depression and religious coping is that as depression worsens, religious faith weakens. Depressed, physically ill persons may lose interest in religion (just as they do in other aspects of life) or may become angry at God for their poor health and dismal situation. Our data, however, provide little support for this explanation. In the follow-up portion of the study, religious coping did not decrease as depressive symptoms increased. If anything, increasing depression tended to be associated with increases in religious coping ($r=0.06$, n.s.). Thus, our data and those of others (36, 37) indicate that when changes in religious coping occur during a period of increasing emotional stress in the context of physical illness, there is no decline in religious coping behavior.

Furthermore, in the longitudinal phase of our study, the baseline religious coping index score was the only sociodemographic or health variable that predicted lower depression scores on follow-up. Although the strength of the relationship was only modest, this finding provides additional evidence that the inverse relation between religious coping and depression in our cross-sectional study might have been due to a buffering effect of religious coping on depression, rather than to an inimical effect of depression on religious coping.

In this study, religious coping was measured with an index made up of both self-rated and observer-rated items. Religion was not defined, other than to say that it might include either belief or activity. However, religion was interpreted as Judeo-Christian by virtually all participants in the study. While this made assessment easier and allowed for high interrater reliability (Pearson's $r=0.81$) on the religious coping measure, it limits the generalizability of these results to religious cognition and behavior in the Judeo-Christian tradition.

Our finding of a high frequency of religious coping among older medical inpatients should alert consultation-liaison psychiatrists and nonpsychiatric health care providers to such behavior and to the possibly use-

ful function it may serve. For elderly persons with health problems and stressful life situations, the immediate aim of psychotherapy is often to support healthy coping behavior (38). Thus, knowledge of strategies that older persons use and find effective in facilitating adjustment is essential. Furthermore, because clinicians may play a role in controlling access to chaplains, religious reading materials, and religious services, identification of patients who rely heavily on religion as a coping behavior is necessary in order to direct resources appropriately.

The inverse relation between religious coping and depression documented here, while only moderate in strength, nevertheless has clinical importance because coping behavior is changeable and, unlike other health variables, can be affected by psychotherapeutic strategies. Religious cognition and behavior may be especially helpful to older patients with severe functional disability and in other situations where a sense of control is lost and other resources are limited. We recognize, however, that while the results of the present study are suggestive, only an intervention trial can definitively establish that religious behavior either prevents or relieves depression in this setting.

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Visual Hallucinations in Patients With Macular Degeneration

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Objective: This study was undertaken to determine the prevalence of visual hallucinations in patients with macular degeneration, describe such hallucinations phenomenologically, and possibly determine factors predisposing to their development. **Method:** Using a case-control design, the authors screened 100 consecutive patients with age-related macular degeneration for visual hallucinations. Each patient with visual hallucinations was matched to the next three patients without hallucinations. The patients and comparison subjects were compared in terms of scores on the Beck Depression Inventory, Eysenck Personality Questionnaire, Telephone Interview for Cognitive Status, and a structured questionnaire including demographic characteristics, family history, and medical and psychiatric history. Ophthalmologic data were obtained by chart review. **Results:** Of the 100 patients, 13 experienced visual hallucinations. Four variables were significantly associated with having hallucinations: living alone, lower cognition score, history of stroke, and bilaterally worse visual acuity. Hallucinations were not associated with family or personal history of psychiatric disorder or with personality traits. In 11 (84.6%) of the 13 patients, the hallucinations had begun in association with an acute change in vision. **Conclusion:** These results indicate that visual hallucinations are prevalent among patients with macular degeneration. They appear unrelated to primary psychiatric disorder. The predisposing factors of bilaterally worse vision and living alone support an association with sensory deprivation, while history of stroke and worse cognition support a decreased cortical inhibition theory.

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Visual hallucinations are associated with a variety of lesions at all levels of the visual system (1-3). Weinberger and Grant (2) reported visual hallucinations in patients with pituitary tumors pressing on the optic nerves and chiasm, noting that the hallucinations were not limited to the area of visual field loss. Lance (4) reported visual hallucinations in patients with homonymous field defects and noted that the hallucinations were confined to the area of visual field loss in all but one patient. Because the calcarine area of the occipital lobe was infarcted in many of these patients, he concluded that it was not the origin of the hallucinations and suggested that the surrounding visual association cortex was. Kolmel (5) reported that 13% of 120 patients with homonymous hemianopia and occipital lobe damage experienced complex visual hallucinations in the hemianopic field. The subjects

stated that the hallucinations occurred hours to days after the loss of vision and disappeared when the hemianopia resolved. He concluded that the hallucinations were "release phenomena" rather than the result of an irritative lesion.

Fitzgerald (6) reported that 15% of 66 patients developed hallucinations within 1 year of becoming blind. He suggested that they were associated with "maladaptive coping" (6, p. 1534) and depression. Lepore (1) examined 104 patients with visual loss due to lesions from the retina to the occipital lobe. He found a 21% prevalence of complex hallucinations or "spontaneous visual phenomena." The severity of the visual acuity loss correlated with hallucinations, but the presence of bilateral as opposed to unilateral disease, older age, or other central nervous system disease did not. He doubted that these hallucinations were associated with psychiatric disorder but did not screen for this.

The eponymous Charles Bonnet syndrome (7-12) has been used to label persistent complex visual hallucinations that occur in the absence of other psychopathology. This syndrome is often associated with eye disease, and insight is fully or partially retained. Most afflicted individuals who have been described were elderly. Controversy exists about whether brain lesions and/or eye

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pathology are necessary to produce this syndrome (7, 9, 13-15).

Many theories to explain hallucinations have been proposed. Jackson (16) proposed that the loss of the inhibiting influence of the cortex releases subcortical activity, producing hallucinations. A related theory (17) is that the reduction of sensory input to specific areas of the brain allows previous perceptions into consciousness as hallucinations. Several lines of data support this hypothesis. A review of sensory deprivation studies (18) indicated that approximately 19% of normal subjects undergoing a variety of sensory deprivation regimens develop visual hallucinations. Interestingly, long periods of isolation were not required; some hallucinations occurred within 48 hours. This theory is also supported by research showing that retinal ganglion cells discharge spontaneously. It has been suggested that decreased sensory stimulation allows these discharges to mimic normal stimuli and are misinterpreted as sensory signals (18).

"Black patch psychosis" (19), a term for delirium associated with patching both eyes after cataract surgery, has been offered as further evidence of the sensory deprivation hypothesis. However, unlike patients with the other conditions discussed, these patients are often delirious, and exogenous factors such as anticholinergic eye drops have not been investigated as causes of delirium.

Other data demonstrate that cortical hyperexcitability or irritability can cause visual hallucinations. Forster (20) found that electrical stimulation of Brodmann areas 17 and 18 of the occipital lobe caused visual sensations, whereas stimulation of area 19 produced complex visual phenomena (figures, people, animals). Penfield and Perrot (21) produced hallucinatory experiences in 7.7% of subjects by stimulating cortical or subcortical structures. The high prevalence of visual hallucinations among people with epilepsy also supports this hypothesis.

As some of the aforementioned studies show, the occipital and temporal lobes are associated with visual hallucinations. Furthermore, hallucinations are frequently present in complex partial seizures, which often originate in the temporal lobe. The more posterior the temporal lobe focus, the more complex the hallucinations (22).

At the neurochemical level the reciprocal roles of the dopaminergic and cholinergic systems may play a part in the induction of visual hallucinations. The treatment of Parkinson's disease with dopamine agonists can produce visual hallucinations and other psychotic phenomena (17, 23-25).

Although visual hallucinations are seen in association with a variety of disorders and occur in normal subjects under special environmental conditions, it is notable that only some people experience them in any one circumstance. Numerous predisposing factors have been postulated. They include psychologic stress (11, 26, 27), suggestibility (28), differences in age or education (29), and cognitive deficits (26, 28, 29). Predisposing personality traits have also been studied (28, 30), and some studies have shown an association between hallucinations

and scores on the neuroticism scale of the Eysenck Personality Questionnaire (28, 31). Barber (32) suggested that a small percentage of people can hallucinate at will.

To further characterize the prevalence and description of complex formed visual hallucinations in patients with visual disorders, we undertook a prevalence and case-control study of individuals with a single ophthalmologic disorder. It was hoped that features predisposing individuals to visual hallucinations could be determined and would suggest theories regarding possible pathophysiology. We chose to study patients with age-related macular degeneration because of reports that they have visual hallucinations (33). Also, age-related macular degeneration is not associated with major systemic changes of the body or brain, as are disorders such as diabetic retinopathy, so it is easier to determine whether the loss of vision is a precipitating factor in the visual hallucinations. Also, the defect in macular degeneration may be measured by visual acuity and disciform scar size. This allowed for a test of the hypothesis that larger lesion size or worse acuity would predispose to the development of hallucinations.

METHOD

One hundred seven consecutive patients who had been diagnosed as having age-related macular degeneration by full-time faculty ophthalmologists at a university retinal vascular center were asked to participate in a study that would involve answering questions regarding their vision. One hundred subjects agreed to participate and gave written informed consent. Once enrolled, each patient was screened for hallucinations by one of two interviewers (S.H., M.C.N.) with the following question: "When people have trouble with their eyes, it frequently affects their vision. It may make it difficult to see things that are there, but sometimes people see things that really are not there or see things that other people don't see. Has this ever happened to you?"

Each subject who responded positively was asked to describe the experience so that illusions, dreams, or vivid thoughts could be excluded by the interviewers. Simple visual experiences such as dots, colors, or flashes of light were not considered to be complex visual hallucinations. Any subject who experienced true complex visual hallucinations underwent a structured interview. Data were collected on age; sex; race; level of education; handedness; living situation; medical history; loss of hearing, taste, or smell; head trauma; delirium; current medicines; family history of neurologic and psychiatric disorders; personal psychiatric history; and substance abuse. All subjects were given the Eysenck Personality Questionnaire (34) and the Beck Depression Inventory (35). The Beck scale was chosen because it has been shown reliable in persons over age 60 (36). The Telephone Interview for Cognitive Status (37), a cognitive screen shown to correlate highly with the Mini-Mental State examination (38) but not depend

TABLE 1. Differences Between Patients With Macular Degeneration Who Did or Did Not Have Visual Hallucinations

Variable	With Hallucinations (N=13)				Without Hallucinations (N=39)				Analysis
	N	%	Mean	SD	N	%	Mean	SD	
Significantly different									
Living alone	7	53.8			8	20.5			$\chi^2=4.76$, df=1, p=0.03
History of stroke	3	23.0			1	2.6			p=0.04 ^a
Bilateral vision of 20/60 or worse	9	69.2			13	13.3			$\chi^2=4.84$, df=1, p=0.03
Score on Telephone Interview for Cognitive Status			30.4	2.6			32.8	2.9	F=6.79, df=1, 50, p=0.01
Score ≤ 33	12	92.3			20	51.3			$\chi^2=6.93$, df=1, p=0.009
Score >33	1	7.7			19	48.7			
Nearly significantly different									
Hearing loss	9	69.2			15	38.5			$\chi^2=3.71$, df=1, p=0.06
Female sex	10	76.9			20	51.3			p=0.10 ^a
Age (years)			77.9	6.0			73.9	7.8	F=2.83, df=1, 50, p=0.10
Vision in best eye			20/91.2	63.9			20/58.5	49.7	F=3.62, df=1, 49, p=0.06

^aFisher's exact test.

on visual or motor capability, was also given. A structured questionnaire was then given to further delineate the phenomenology of the visual hallucinations. A copy of the interview instrument can be obtained from the authors.

The case-control method was chosen to identify predisposing factors for hallucinations because the prevalence of positive cases was unknown and a low prevalence was suspected. After each positive case was identified, the next three hallucination-negative patients were identified as comparison subjects and were given the same battery except for the questionnaire further delineating the phenomenology of the visual hallucinations.

Data regarding the patient's visual diagnosis, visual acuity, disciform scar size, and laser treatment history were abstracted from the chart by one of us, an ophthalmologist (D.F.).

The data were analyzed by using the following statistics: Fisher's exact test, chi-square analysis, analysis of variance, logistic regression, and discriminant analysis. The obtained p values were used to assess the strength of association of the variables with the presence of visual hallucinations rather than to test a formal hypothesis. Therefore, no correction for multiple comparisons was used.

Nonadjusted relative risks were calculated for the variables that distinguished the patients with hallucinations and the comparison subjects. Adjusted relative risks were calculated by logistic regression.

RESULTS

Thirteen of the 100 patients screened positive for visual hallucinations, giving a prevalence of 13%. Thirty-nine hallucination-negative patients served as comparison subjects.

The mean age of the 52 subjects was 74.9 years (SD=7.5); 86.6% were white (N=45), and 42.3% were male (N=22) and 57.7% were female (N=30). The mean education level was 12.5 years (SD=2.5). The mean visual acuity was 20/105 for either eye (SD=78.5).

As shown in table 1, the hallucinators differed significantly from the comparison subjects on the variables of living alone, having a personal history of stroke, having bilateral visual acuity of 20/60 or worse, and score on the Telephone Interview for Cognitive Status. A score of 33 on the Telephone Interview for Cognitive Status was used to divide the groups into those with better and worse cognition. This score was chosen because the distribution of scores was bimodal. The hallucinators were more likely to score 33 or less (table 1).

Several variables showed nearly significant differences between the patients with and without hallucinations (table 1). These variables were hearing loss, female sex, age, and visual acuity in the patient's best eye. This last variable was used as a measure of best acuity.

Logistic regression and discriminant function analysis were used to identify a model of variables that could best predict whether a patient with macular degeneration would or would not have visual hallucinations. A four-factor model (using the four significant variables of living alone, history of stroke, lower score on the Telephone Interview for Cognitive Status, and bilateral vision of 20/60 or worse) determined by logistic regression gave the overall best prediction of 87.8%. It correctly classified 61.5% of the hallucinators and 97.2% of the comparison subjects. Discriminant analysis was performed on the four significant variables as well as the four variables that showed nearly significant differences (hearing loss, female sex, older age, worse visual acuity in the best eye) but resulted in a lower overall predictive value than did the logistic regression. The adjusted and nonadjusted relative risks for the significant variables and the nonadjusted relative risks for the nearly significant variables are shown in table 2.

Also of interest were the variables found not to be significantly different between the hallucinators and comparison subjects. These included level of education, handedness, number of concurrent medical disorders, loss of taste or smell, history of head trauma or delirium, number of medications, drug and alcohol use (past or current), family or personal history of neurologic disorder (Parkinson's disease, stroke, epilepsy, or de-

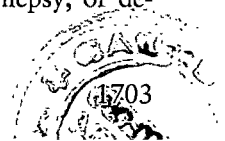


TABLE 2. Nonadjusted and Adjusted Relative Risks for Visual Hallucinations in 52 Patients With Macular Degeneration

Variable	Nonadjusted Relative Risk		Adjusted Relative Risk ^a	
	Risk	95% Confidence Interval	Risk	95% Confidence Interval
Living alone	4.23	1.10-16.19	2.48	0.47-113.14
History of stroke	11.40	1.07-121.70	15.50	0.89-270.5
Lower score on Telephone Interview for Cognitive Status	11.40	1.35-96.34	13.05	0.97-175.75
Bilateral vision of 20/60 or worse	4.33	1.12-16.78	4.59	0.85-24.91
Hearing loss	3.60	0.94-13.79		
Female sex	3.16	0.75-13.29		
Older age	2.37	0.62-9.00		
Worse vision in best eye	3.32	0.87-12.67		

^aDetermined by logistic regression using a four-variable model (living alone, history of stroke, lower cognition score, bilateral vision of 20/60 or worse).

mentia), and family or personal history of psychiatric disorders (affective disorder, schizophrenia, anxiety, or other). There were no differences between the hallucinators and the comparison subjects in scores on the Beck Depression Inventory or Eysenck Personality Questionnaire. There were no differences in history of laser treatment to eyes or disciform scar size.

Characteristics of the hallucinations are shown in table 3. The patients saw a wide variety of hallucinations; some patients saw only one form, whereas others saw many different forms. They included animals, people, both full bodies and faces, scenery, objects, and geometric shapes. Examples include "elaborate rows of Victorian houses, with pastel colors," "frightening faces with brown hair that would grow to cover the face," "a collie dog," "moving gold chains," "red brick buildings," "groups of brown-red squares," "groups of men wearing elaborate fifteenth-century garb," and "two militarized teams of men playing football."

The period during which the patients had seen these hallucinations ranged from 2 to 36 months at the time of the interview. Eleven subjects (84.6%) reported an acute change in vision coincident with the beginning of the hallucinations, while two (15.4%) described an insidious onset. Three (23.1%) noted that the hallucinations always occurred during the same time of day. Three (23.1%) found they occurred more often in bright light, two (15.4%) said they occurred more often in dim light, and eight (61.5%) found no difference. Four (30.8%) could make the hallucinations temporarily go away by blinking, one (7.7%) could do so by trying to focus on the hallucinations, and eight (61.5%) were unable to affect the hallucinations. No patient could induce a hallucination.

None of the visual hallucinations were accompanied by a hallucination in another sense (auditory, olfactory, tactile, or gustatory). Although all of the subjects believed that the hallucinations were related to their eye

TABLE 3. Characteristics of Visual Hallucinations in 13 Patients With Macular Degeneration

Hallucination Characteristic	Patients	
	Number	Percent
Size		
Normal	10	76.9
Abnormal	3	23.1
Color		
Normal	9	69.2
Abnormal	2	15.4
Variable	2	15.4
Transparency		
Solid	9	69.2
Transparent	3	23.1
Variable	1	7.7
Definition of edges		
Sharp	12	92.3
Blurry	1	7.7
Movement		
Moves	7	53.8
Stands still	5	38.5
Variable	1	7.7
Appearance relative to other things		
As real	11	84.6
Not as real	2	15.4
Familiarity of objects		
Seen before	6	46.2
Unfamiliar	5	38.5
Both	2	15.4
Frequency		
Daily	7	53.8
Weekly	2	15.4
Monthly	3	23.1
Don't know	1	7.7
Present frequency relative to past frequency		
Same	7	53.8
More often	1	7.7
Less often	4	30.8
Don't know	1	7.7
Duration		
Minutes	6	46.2
Hours	3	23.1
Days	1	7.7
Variable	3	23.1
Presence in area of visual loss		
Yes	7	53.8
No	4	30.8
Both	2	15.4
Presence in same area of visual field on different occasions		
Yes	12	92.3
No	1	7.7

disorder three (23.1%) had occasionally acted on the hallucination (e.g., tried to touch it, push it away). Citing reasons such as fearing "others would think [they were] crazy," three (23.1%) had never told anyone of these experiences before this study. Of the 10 (76.9%) who had told someone, five had told their doctors.

DISCUSSION

The occurrence of complex visual hallucinations in patients with age-related macular degeneration is not uncommon, and a prevalence of 13% was found in this

consecutive group of patients. This is important to know as some patients will not tell anyone, including their doctors, unless asked. Many patients expressed relief at knowing that others had this experience and that doctors were trying to study this phenomenon. The results of this study might reassure patients and teach physicians that having visual hallucinations with age-related macular degeneration is not associated with depression, other primary psychiatric disorder, or abnormal personality.

Given that neurologic diseases such as epilepsy, dementia, and Parkinson's disease are associated with visual hallucinations, it was interesting that these disorders were not found among our hallucinators. Similarly, alcohol and drug use, number of medications, and number of medical disorders were not associated with the hallucinations. This suggests that these variables were not the cause of visual hallucinations in patients who happened to also have age-related macular degeneration. Also, factors suggested by previous studies as associated with hallucinations, such as education, depression, and personality traits (especially score on the Eysenck Personality Questionnaire neuroticism scale), were not supported in this study. No support was found for patients' "hallucinating at will."

The close association noted by the hallucinators between a sudden change in vision (due to laser treatment, hemorrhage, etc.) and the onset of the hallucinations also suggests that the visual hallucinations were related to the visual disorder. Further, the facts that bilateral visual acuity of 20/60 or worse was significantly associated with hallucinations and that the hallucinators had somewhat worse vision in the best eye suggest a relationship between the severity of eye disease and the phenomenon of hallucinations. However, since only 13% of the patients with age-related macular degeneration experienced visual hallucinations and since no risk factor distinguished 100% between the hallucinators and the nonhallucinators, the variables found to be significantly different between the hallucinators and comparison subjects might best be considered predisposing factors.

The theory of sensory deprivation is supported by the findings of bilateral as opposed to unilateral disease and more severe visual impairment among the subjects with hallucinations. Also, half of the hallucinations were limited to the area of visual field loss, i.e., the area of sensory deprivation. Living alone, although less clearly related, might also be linked with less sensory stimulation. The nearly significant association between hearing loss and hallucinations also supports a sensory deprivation model, as one more route of sensory input is reduced.

Two risk factors identified here, lower cognition score and personal history of stroke, support the hypothesis that decreased cortical inhibition allows subcortical or adjacent cortical areas to "release" discharges, causing hallucinations. Our results also support previous studies linking cognitive deficits with hallucinations (26, 28, 29). Furthermore, cognitive deficits in Parkinson's disorder patients have also been associated with

risk of hallucinations (25). A study of patients with Charles Bonnet syndrome (7) revealed that two of six subsequently developed dementia, which raises the question of whether visual hallucinations in patients with age-related macular degeneration may be a risk factor for or, more likely, an early symptom of dementia. A follow-up study of these patients may answer this question. The nearly significant association between older age and hallucinations could also indicate that greater age-related cortical atrophy is a risk factor, but we have no data to support or refute this possibility. The work of Foerster (20), who produced complex visual hallucinations by stimulating the visual association cortex, makes visual association cortex area 19 a possible candidate for the brain region "releasing" visual hallucinations. Interestingly, an abnormally high number of neurofibrillary tangles are found in the visual association cortex of patients with Alzheimer's disease (39), a disease in which 10% of patients have visual hallucinations, with relative sparing of the primary visual cortex (40).

An examination of phenomena in other visual disorders and over a broader age range is now underway. This may help clarify the importance of age as a risk factor, since all our patients were over age 55. It will also help clarify whether this phenomenon is present in visual disorders with different pathologies and further define other factors found in this study to be associated with hallucinations. To clarify whether cortical atrophy or cortical hyperexcitability is a risk factor, it would be helpful to study brain structure (with magnetic resonance imaging and computerized tomography) and function (with EEG, visual evoked potentials, single photon emission computed tomography, and positron emission tomography).

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Elderly Israeli Holocaust Survivors During the Persian Gulf War: A Study of Psychological Distress

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***Objective:** The aim of the current study was to systematically assess the psychological effects of the Persian Gulf War on a nonclinical group of elderly Israeli civilians with and without a Holocaust background. **Method:** Sixty-one elderly Holocaust survivors and 131 elderly civilians without a Holocaust background completed questionnaires in their homes. Measures included sense of safety, symptoms of psychological distress, and levels of state and trait anxiety. **Results:** Findings indicate that Holocaust survivors perceived higher levels of danger and reported more symptoms of acute distress than comparison subjects. In addition, they displayed higher levels of both state and trait anxiety. **Conclusions:** Findings do not support the notion that prior experience with extreme stress has an inoculating effect that leads to greater resilience in dealing with other forms of stress. On the contrary, Holocaust experience was found to render the elderly more vulnerable rather than less. These findings of greater vulnerability among Holocaust survivors are of particular significance since they stem from a nonclinical group.*

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Over a period of 6 weeks, from mid-January to the end of February 1991, the residents of Israel were exposed to a war in which 39 Iraqi Scud missiles, not aimed at military targets, fell in the heart of civilian residential areas. The citizens of Israel were required to equip themselves with masking tape, plastic sheeting, wet towels, and baking soda and were issued gas masks to protect themselves against the Iraqi threat to use biological and chemical weapons. Life in Israel carried on in what became known as the "emergency routine," that is, an ongoing series of emergency alerts separated by hours or days of relative calm. Some places, primarily those providing vital services, remained open in the mornings, but social and cultural activities were almost completely curtailed so as to avoid large gatherings. In the late afternoon, most people retired to their homes, close to their sealed rooms and gas masks, and nervously readied themselves for nighttime, when the missiles would fall.

Despite the fact that millions of people around the globe have been exposed in this century to the horrors of war, and although there have been many studies of war-induced stress, relatively few have focused on civil-

ians. There are a few pioneering works (1, 2), but these have primarily been either impressionistic or based on small samples. Research on high-risk segments of the population are particularly lacking. The present study examined the responses of one group that was identified during the war as being at high risk for psychological distress: the elderly.

Approximately 10% of the population of Israel is over age 60, and in the greater Tel Aviv area (the area that sustained the most missile attacks during the war), the elderly constitute around 14% of the population. While many younger people left the city during the war in search of safer areas, most of the elderly remained at home. Certain aspects of the war were especially distressing for the elderly: community support activities were drastically curtailed during the war and senior citizens' centers were closed, since people refrained from leaving home when not absolutely necessary. Protective devices such as gas masks, which require a certain amount of manual dexterity, also posed problems for many of the elderly. For those with impaired vision or hearing, seclusion in the sealed room often aggravated their sense of isolation from the outer world. Fear of not hearing the warning sirens or difficulty in understanding the emergency instructions broadcast over the media distressed and worried many. These difficulties were especially severe among those who lived alone; their loneliness was exacerbated during the war.

While the war was stressful for all the elderly in Israel, there was one group in particular whose prior life experiences might be expected to affect their responses

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to the current crisis: Holocaust survivors. Many of this group who immigrated to Israel after World War II seemed, at least outwardly, to have overcome the horrors of their past. Most have raised families and have led productive and full lives. Some of them, however, are haunted by the past and remain scarred by posttraumatic stress (3). The literature is divided with regard to the extent and depth of long-range impairment resulting from the Holocaust. On the one hand, some claim that the Holocaust left a permanent mark and that a large percentage of survivors suffer from severe and debilitating disorders such as chronic anxiety and depression (4) or personality constriction (5). On the other hand, others believe that severe disorders are to be found only among a minority and that most survivors do not manifest serious psychological impairment. On the contrary, most of them lead productive lives despite their ordeal (6).

There is, however, consistent evidence that people who undergo extreme stress are left more vulnerable and more sensitive to *future* adversity (7). Moreover, even people who have seemingly overcome their traumatic experiences may suffer from heightened vulnerability in the future (8) and in extreme cases from reactivation of acute stress responses following exposure to stimuli that symbolize or recall the original traumatic experience (9). The work of Christenson and colleagues (10) is especially relevant in this regard. They examined reactivation of posttraumatic reactions among the elderly. In their work they found that life events such as retirement, children leaving home, death of a loved one, and other stressful events served as triggers that accelerated and unmasked latent posttraumatic stress disorder (PTSD) among American World War II combat veterans.

Clinical impressions indicate that while the Persian Gulf War was stressful for all the population of Israel, it was an especially painful reminder for the Holocaust survivors. The feeling of being "sitting ducks," the sense of impending doom, the threat to use gas (purchased in Germany), and the rows of decontamination showers positioned at the entrance to every hospital (which reminded the survivors of the entrance to the gas chambers in the concentration camps) all made the war particularly stressful for the Holocaust survivors.

The aim of the current study was to systematically assess the psychological effects of the Persian Gulf War on elderly civilians with and without a Holocaust background. Specifically, we examined sense of safety, symptoms of psychological distress, and levels of state and trait anxiety.

METHOD

Subjects

A total of 192 subjects participated in this study. Sixty-one (31.8%) were Holocaust survivors and 131 (68.2%) did not have this background. In the Holocaust group, the mean age was 68.3 (SD=7.2) and 33.3%

(N=20) were men. In the non-Holocaust group, the mean age was 72.9 (SD=7.5) and 38.5% (N=50) were men. Thirty-six percent of the subjects lived in kibbutzim (communal settlements), and the remaining 64% resided in cities in the center of Israel. Five percent of the subjects were born in Israel, and the remainder were of European origin. Seventeen percent of the respondents had completed elementary school, 53% had finished high school, and 30% had studied beyond high school. Fifty-seven percent were married at the time of the study, 37% were widowed, 2% were divorced, and 4% had never married. Sixty-six percent of the respondents described themselves as secular, 26% as traditional, and 8% as orthodox. Twelve percent were residents of an urban community home for the aged; the remainder lived in their own homes, whether in kibbutzim or in cities.

Procedure

In each community, a local social worker who was well acquainted with the elderly residents of the area and experienced in working with this population was recruited to administer questionnaires. The social worker approached potential subjects and requested their consent to participate in the study. Subjects completed the questionnaires in the presence of the social workers, who answered questions as necessary.

Subjects were first presented with a brief questionnaire inquiring about sociodemographic variables such as age, sex, education, religious observance, marital status, place of residence, country of origin, and current health status. Subjects were then queried in detail about prior traumatic experiences, such as internment in concentration camps during World War II, participation in wars, loss of loved ones, and personal life events. Subjects were also asked to note if they had experienced any event similar to the Persian Gulf War in the past.

Sense of safety. Subjects were asked to rate their level of personal safety during the war in a number of different areas on a scale ranging from 1 (not at all) to 5 (very much). Internal validity of the nine-item questionnaire was examined through factor analysis with varimax rotation. This analysis yielded three principal factors (eigenvalue greater than 1) that explained 62.6% of the variance.

In the current study, we employed only the first factor, which explained 31.0% of the variance and related to the subjects' perceptions of danger. This factor includes questions such as "To what degree do you feel that your life is in danger?" "To what degree do you assess that the country of Israel is in danger of being annihilated?" and "To what degree do you think that your family is in danger?"

State-Trait Anxiety Inventory. This questionnaire (11) is a standardized measure of anxiety that has been used frequently in studies of traumatic stress throughout the world, particularly with civilian populations, thus allowing for comparisons with other samples (2). It is composed of two 20-item scales. The State Anxiety

scale assesses the person's *current* or transitory emotional state, and the Trait Anxiety scale examines the way the subject *generally* feels.

Psychological Distress in Wartime. This self-report measure, devised for the current study, comprises 19 items all of which examine typical responses to extreme stress. Unfortunately, no standardized criteria for assessment of acute stress reactions are currently available, and even the most recent diagnostic and statistic manual, *DSM-III-R*, does not include a relevant category. The closest and most relevant nosological category in *DSM-III-R* is that of PTSD. The symptoms required for diagnosis of PTSD (e.g., distancing from others, nightmares, startle response, hypervigilance) were, therefore, chosen as the basis for most of the items in this questionnaire. Since this assessment was conducted *during* rather than after the exposure to the stressor, however, not all of the *DSM* criteria were appropriate, and, of course, the criterion of 1-month duration could not be met. For this reason, no attempt was made to address the issue of diagnosis. Subjects were asked to rate the presence of each symptom in the past week on a 4-point scale ranging from 1 (not at all) to 4 (very often). The mean score on this scale was 36.4 ($SD=11.7$). In order to examine internal consistency, Cronbach's alpha was calculated and was found to be high (0.90).

RESULTS

In order to examine differences between subjects with and without a Holocaust background, a multivariate analysis of the four dependent variables was conducted. The analysis indicated a large and significant effect ($F=8.14$, $df=4$, 109, $p<0.001$). All four dependent variables were significantly different between the two groups (all p values were <0.001); elderly Holocaust survivors perceived significantly higher levels of danger, experienced more emotional distress, and had higher levels of both state and trait anxiety than subjects without a Holocaust background.

In order to examine whether there were differences in background variables between the two groups, a multivariate analysis of variance (MANOVA) was performed with the sociodemographic characteristics (age, sex, education, religiosity, health status, and proximity to bomb sites) as independent variables and Holocaust background as the dependent variable. This analysis yielded a significant main effect ($F=10.19$, $df=6$, 173, $p<0.001$) because of the fact that the Holocaust survivors were significantly younger ($F=21.51$, $df=1$, 179, $p<0.001$), less educated ($F=14.37$, $df=1$, 179, $p<0.001$), and more religious than the other subjects ($F=12.88$, $df=1$, 179, $p<0.001$) and were closer to the bomb sites ($F=16.00$, $df=1$, 179, $p<0.001$). It was therefore decided to perform the MANOVA on the dependent variable with the background variables as covariates. Table 1 presents the means and standard deviations of the four dependent variables separately for

TABLE 1. Psychological Ratings During the Persian Gulf War for Elderly Israeli Survivors of the Holocaust and Other Elderly Subjects^a

Measure	Holocaust Survivors (N=61)		Other Subjects (N=131)		F (df=1, 100)
	Mean	SD	Mean	SD	
Perceptions of danger	-0.2	0.9	0.5	1.1	2.29
Psychological distress	42.9	11.9	33.0	10.1	6.20
State anxiety	47.4	13.2	36.5	13.0	6.27
Trait anxiety	50.3	10.4	41.5	7.4	7.53 ^b

^aA multivariate analysis of covariance was performed with age, sex, education, religiosity, health, and proximity to bomb sites as covariates. Overall $F=2.43$, $df=4$, 97, $p<0.05$.

^b $p<0.05$, with Bonferroni correction (12) for multiple comparisons.

Holocaust survivors and the other respondents and the results of the multivariate analysis, covarying for the background variables.

As can be seen in table 1, the effect of the Holocaust was marginally significant ($p<0.05$) after the effects of the background variables were removed. When the structure of the relationships was examined with univariate analyses, we found that perception of danger was not significantly different between the two groups. In univariate analyses of variance we found that state anxiety and psychological distress were different between the two groups ($p<0.05$). These significance tests should be interpreted cautiously because multiple comparisons were performed. We therefore performed a more conservative estimate of the significance level, using the Bonferroni correction (12), and found that the two groups did not differ significantly. Trait anxiety was significantly different between the two groups after the background variables were covaried ($p<0.05$, with Bonferroni correction).

In sum, results show that even after a wide range of background variables were controlled, there were still marginally significant differences between the Holocaust survivors and the other elderly civilians, with the Holocaust survivors experiencing more difficulties than the other subjects.

DISCUSSION

The findings of this study indicate that elderly survivors of the Holocaust suffered considerable emotional distress during the Persian Gulf War. It should be noted that differences between the Holocaust survivors and the other elderly subjects were evident even when a most conservative analysis of the data was conducted that controlled for a wide range of background variables, some of which may themselves have been a function of Holocaust experiences (e.g., health status).

These findings do not support the notion that prior experience with extreme stress has an inoculating effect that leads to greater resilience in dealing with other forms of stress. Norris and Murrell (13), for example,

studied a large sample of elderly flood victims and found evidence for both direct tolerance (exposure to a particular stressor reduces the subsequent impact of the *same* stressor) and cross-tolerance (exposure to one type of stressor lowers the pathogenicity of a *different* stressor). In the current study, however, there were no such effects. On the contrary, Holocaust experience was found to render the elderly *more* vulnerable rather than less. In fact, using a cutoff point of 44 on the Trait Anxiety scale, as suggested by Himmelfarb and Murrell (14), we found that a large proportion of the Holocaust survivors (51%) were at risk for a "degree of psychological distress that would require intervention" (14, p. 162). Moreover, the proportion of Holocaust survivors with Trait Anxiety scale scores above the cutoff point was more than *double* that of the other subjects (24%).

These findings are consistent with those of prior studies that have demonstrated greater vulnerability to stress among trauma victims. Prior studies by this group (9), for example, have found that the greater the similarity between two traumatic events, the greater the chance for a reactivation of the original stress response after the second event. It should be kept in mind, however, that even a very different stressor may lead to reactivation of an earlier stress response among the elderly (10).

There is some controversy in the literature with regard to the long-term effects of the Holocaust on survivors. Titchener (15, 16) has suggested that a process of posttraumatic decline may take place in the years after exposure to a traumatic event and that permanent characterological effects of the trauma may be observed, particularly in terms of proneness to anxiety reactions. Niederland (4) has characterized the "survivor syndrome" as a chronic state of anxious bland depression. One major limitation of most reports on Holocaust survivors has been that formulations of the survivor's adjustment during and after internment have been based primarily on analysis of individuals who were seeking help for emotional problems. Few studies have used normal samples. Researchers such as Leon and colleagues (6) have claimed that generalizations about survivors as a group were based on the analysis of clinical cases and have questioned the generality of these findings. In fact, community studies have often failed to uncover significant pathology among Holocaust survivors.

The current findings of both acute stress and higher levels of state (acute) and trait (characterological) anxiety are, therefore, of significance, since we used a normal group as well as a comparison group of the same ethnic and cultural background as the survivors.

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Utilization of Neuropsychiatric Diagnostic Tests for General Hospital Patients With Mental Disorders

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Objective: The author's goal was to determine the frequency and distribution of neuropsychiatric diagnostic tests provided to general hospital patients with mental disorders. **Method:** Data from the 1989 National Hospital Discharge Survey were analyzed to determine the number, proportion, and general characteristics of 11,628 discharged patients with primary diagnoses of mental disorders who underwent computerized tomography (CT) scanning of the head, EEG, and magnetic resonance imaging (MRI) of the brain. **Results:** Of the discharged patients with mental disorders, 5.1% had received CT scans, 2.8% had received EEGs, and 0.7% had received MRI. These rates were below the rates for patients discharged with primary diagnoses of neurological disorders but above the rates for patients discharged with primary diagnoses of other medical disorders. Among the patients discharged with mental disorder diagnoses, the likelihood of receiving a CT scan or an EEG was greater if the primary diagnosis was an organic disorder or if the secondary diagnosis was a medical disorder. Patients over age 65 were also more likely to have received a CT scan. Hospital size and location had a modest influence on the likelihood of receiving a CT scan or EEG, but the ownership of the hospital and the patient's source of payment were not significant influences. **Conclusions:** Neuropsychiatric diagnostic testing is selectively utilized in the routine treatment of general hospital psychiatric inpatients. Clinical variables rather than institutional or financial variables appear to be the most powerful predictors of which patients are selected to receive these tests.

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General hospitals have assumed a leading role in acute inpatient psychiatric care (1). According to recent national estimates, general hospitals account for more than half of all psychiatric inpatient admissions (2). In relation to this large commitment of resources, surprisingly little is known about the composition of routine care. This article focuses on one aspect of psychiatric practice in general hospitals: the utilization of neuropsychiatric diagnostic procedures.

Patient assessment remains a major task in psychiatric hospitalization (3, 4). Because psychiatric symptoms are often early manifestations of remediable central nervous system (CNS) disease, psychiatric assessment commonly includes an effort to uncover brain pathology (5, 6). Anatomic and functional brain imaging technologies play an important role in this process. EEG, computed tomography (CT), and magnetic resonance

imaging (MRI) are three procedures capable of providing information that dramatically focuses clinical management on underlying CNS disease (7-9).

Enthusiasm for technologically sophisticated diagnostic procedures has been tempered by concerns about rising medical costs. Fiscal control of technology has been targeted as an important means of slowing the ever-increasing cost of health care (10). Concerns about rising health care costs have led researchers to examine the clinical yield of various diagnostic procedures. In the case of CT scans of the head and EEGs, research with psychiatric inpatients suggests that indiscriminate testing has limited clinical utility and may be an inefficient use of precious medical resources (11-13). In the absence of clear clinical indications, CT scanning and EEG rarely lead to the detection of previously unknown organic disease or changes in patient treatment. Clinical research further suggests that MRI of the brain should be ordered only when there is strong suspicion of gross neuropathology (14).

The rate and pattern of neuropsychiatric diagnostic testing for hospitalized patients with mental disorders have received scant attention. Previous research in this area has been limited to utilization reviews at individual hospitals. These hospitals are typically large urban uni-

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versity facilities. Because clinical practice at these facilities may not be representative of general patterns of care, this research may not accurately portray broader trends in practice. A more accurate assessment of inpatient practice requires a nationally representative sample of inpatient test utilization.

Previous research suggests that the rate of neuropsychiatric test utilization varies by treatment setting. Depending upon the setting, rates of CT head scanning for psychiatric inpatients have been reported to range from 3% to 100% (8, 11, 15, 16) and rates of EEG to vary from 18% to 33% (13, 17). At present, there is little information on the utilization of MRI technology for inpatients with mental disorders.

This study is the first exploration of the utilization of CT head scanning, EEG, and MRI of the brain for a nationally representative sample of general hospital inpatients with mental disorders. The results suggest that neuropsychiatric diagnostic procedures are provided to only a small proportion of general hospital inpatients with mental disorders and that clinical variables rather than institutional or financial variables are of greatest importance in determining test utilization.

METHOD

The data for this report were drawn from the 1989 National Hospital Discharge Survey (18), a nationwide survey of inpatient utilization conducted by the National Center for Health Statistics. The survey selects a national probability sample of patients discharged from non-federal-government hospitals whose average length of stay is less than 30 days. Because over 95% of these facilities are general hospitals, they are referred to as such in this report.

The National Hospital Discharge Survey is conducted by means of a three-stage sampling design. The first stage involves selecting a probability sample of primary sampling units. The second stage involves selecting all hospitals within the chosen primary sampling units that have 1,000 or more beds or 40,000 or more annual discharges and selecting a probability sample of smaller hospitals. The third stage involves selecting discharges from the chosen hospitals by a systematic random-sampling technique. This strategy oversamples frequent users of inpatient care, but it accurately reflects overall provision of inpatient care in short-stay hospitals other than those run by the federal government.

The National Hospital Discharge Survey consists of data abstracted from the face sheets of patients' medical records. The abstracted data include demographic information, discharge status, length of hospital stay, discharge diagnoses, and inpatient procedures. Discharge diagnoses and procedures are reported according to the ICD classification system.

The survey also provides information on hospital size, geographic location, and ownership. Geographic location is reported for the four regions of the United States used by the U.S. Bureau of the Census. Owner-

ship of hospitals is reported in three broad categories: proprietary, not-for-profit, and government. Because general hospitals operated by the federal government are outside the scope of the National Hospital Discharge Survey, surveyed government facilities are limited to hospitals operated by state or local governments.

Discharges are divided into those for which the primary discharge diagnosis was a mental disorder (ICD-9-CM codes 290-319), those for which the primary discharge diagnosis was a neurological disorder (ICD-9-CM codes 320-359), and those for which the primary discharge diagnosis was a medical disorder (ICD-9-CM codes 001-289, 360-999, and V01-V82). Most of the analyses concern discharges with primary mental disorder diagnoses.

This report focuses on the utilization of three diagnostic procedures: CT scan of the head (ICD-9-CM procedures code 97.03), EEG (code 89.14), and MRI of the brain (code 88.91). Some analyses involve aggregating patients with mental disorders into six groups on the basis of their primary discharge diagnoses. These groups include organic disorders (codes 290, 293, 294, 310), schizophrenic disorders (code 295), affective disorders (codes 296, 311, 298.0), drug- and alcohol-related disorders (codes 291, 292, 303-305), neurotic disorders (code 300), and other disorders (codes 297, 298.1-299, 301, 302, 306-309, 312-319). These diagnostic groupings are a modification of those developed by the National Institute of Mental Health (19).

A weighting system has been developed by the National Center for Health Statistics to produce national estimates from National Hospital Discharge Survey sample estimates (18). The construction of the patient weights is based on inflation by the reciprocal of sampling probability. The percentages provided in this report are based on weighted estimates.

Logistic regressions were used to estimate the likelihood (relative risk) that patients discharged with primary diagnoses of mental disorders would have received a CT scan of the head or an EEG during their hospital stay. Results are presented as odds ratios with associated 95% confidence intervals. These computations were made with unweighted data.

Because the sample survey contained a relatively small number of discharged patients with primary mental disorder diagnoses who received an MRI of the brain (N=62), only limited analyses of these discharges are presented.

RESULTS

Frequency of Diagnostic Testing

Table 1 presents the frequency of CT scans of the head, EEGs, and MRI of the brain for general hospital inpatients with primary diagnoses of mental disorders, neurological disorders, and medical disorders. Of the estimated 1.51 million patients discharged from U.S. general hospitals in 1989 with primary diagnoses of mental disorders, ap-

TABLE 1. Frequency of Selected Diagnostic Procedures Provided to Inpatients Discharged From General Hospitals With Three Groups of Primary Diagnoses^a

Procedure	Patients With Mental Disorders			Patients With Neurological Disorders			Patients With Medical Disorders		
	National Estimate (1,514,200)	%	Study Sample (N=11,628)	National Estimate (431,700)	%	Study Sample (N=3,030)	National Estimate (32,885,300)	%	Study Sample (N=218,835)
CT scan of the head	77,900	5.1	624	62,900	14.6	508	686,500	2.1	5,865
EEG	42,700	2.8	346	34,400	8.0	268	161,800	0.5	1,307
MRI of the brain	10,000	0.7	62	16,400	3.8	129	72,300	0.3	654

^aData are from the 1989 National Hospital Discharge Survey (18). Federal government hospitals are not included. Mental disorders are defined as ICD-9-CM codes 290–319, neurological disorders as codes 320–359, and medical disorders as all other ICD-9-CM codes. Percentages are based on weighted sampling.

proximately 78,000 (5.1%) had received CT scans of the head, 43,000 (2.8%) had received EEGs, and 10,000 (0.7%) had received MRI of the brain.

Patients with mental disorders tended to undergo neuropsychiatric procedures less frequently than patients with neurological disorders but more frequently than patients with other medical disorders. Patients with mental disorders were less than half as likely as patients with neurological disorders to receive either a CT scan or an EEG and less than one-fifth as likely to receive MRI. At the same time, patients with mental disorders were more than twice as likely as patients with other medical disorders to receive a CT head scan or MRI and more than five times as likely to receive an EEG (table 1).

The vast majority (93.2%) of patients discharged from general hospitals with diagnoses of mental disorders did not undergo any of the three neuropsychiatric procedures. Overall, patients with mental disorders accounted for only a modest proportion of the neuropsychiatric tests ordered for patients discharged from general hospitals (17.9% of the EEGs, 10.1% of MRI of the brain, and 9.4% of the CT head scans).

Patients with mental disorders who received any one of the diagnostic tests were likely to receive others. More than one-quarter (30.4%) of the patients with mental disorders who had a CT scan of the head also had either an EEG or MRI of the brain. More than one-third (44.4%) of the patients with mental disorders who underwent MRI also had either a CT scan or an EEG. Over one-half (60.3%) of the patients with mental disorders who received an EEG also received either a CT scan or MRI.

Demographic Characteristics and Sources of Payment

Selected demographic characteristics of the patients with mental disorders who received CT scans of the head or EEGs are presented in table 2. Patients who received CT scans of the head tended to be older than patients who received EEGs, and patients who received EEGs tended to be older than those who did not undergo either procedure. Over one-third (40.6%) of the patients with mental disorders who received CT scans of the head and nearly one-quarter (23.2%) of those who received EEGs were over 65 years of age.

TABLE 2. Demographic Characteristics of Inpatients Discharged From General Hospitals With Primary Diagnoses of Mental Disorders, Grouped According to Selected Diagnostic Procedures^a

Characteristic	Patients Who Had CT Scans of the Head (N=624)		Patients Who Had EEGs (N=346)		Patients Who Had Neither Procedure (N=10,850)	
	N	%	N	%	N	%
Sex						
Female	303	47.7	170	43.6	5,070	48.3
Male	321	52.3	176	46.4	5,780	41.7
Age (years) ^b						
<18	32	3.0	44	10.4	827	8.3
18–35	145	20.1	99	25.0	4,709	40.7
36–50	127	21.6	80	24.4	2,840	24.7
51–65	95	14.7	53	17.0	1,247	12.8
>65	225	40.6	70	23.2	1,221	13.5
Race						
White	441	71.9	237	64.3	7,920	75.1
Black	118	16.3	73	20.7	1,969	14.9
Other	65	11.8	36	15.0	961	10.0

^aData are from the 1989 National Hospital Discharge Survey (18). Percentages are based on weighted sampling.

^bFor patients who had CT scans of the head, mean=52.8 years (SD=22.8); for patients who had EEGs, mean=43.9 years (SD=22.1); for patients who had neither procedure, mean=39.1 years (SD=17.9).

For patients with mental disorders, the most common primary source of payment for hospitalization was private insurance (36.7%). Medicare (23.9%) and Medicaid (19.2%) were also common sources of payment. Self-pay (10.5%) and other sources (9.7%) were less common.

CT scans of the head were provided to 9.9% of Medicare patients with mental disorders, 5.1% of self-paying patients, 3.8% of Medicaid patients, and 3.3% of privately insured patients. EEGs were provided to 4.1% of self-paying patients with mental disorders, 3.6% of Medicare patients, 3.0% of Medicaid patients, and 2.3% of privately insured patients.

Discharge Status

A majority of the general hospital inpatients with mental disorders (79.1%) received routine discharges. A

TABLE 3. Frequency of CT Scans of the Head and EEGs Provided to Inpatients Discharged From General Hospitals With Primary Diagnoses of Selected Groups of Mental Disorders^a

Procedure	Organic Disorders (N=613)		Schizophrenic Disorders (N=1,690)		Affective Disorders (N=2,996)		Drug- and Alcohol-Related Disorders (N=3,792)		Neurotic Disorders (N=707)		Other Disorders (N=1,830)	
	N	%	N	%	N	%	N	%	N	%	N	%
CT scan of the head	143	20.0	62	3.7	145	4.0	134	4.1	32	4.2	108	5.1
EEG	54	8.0	46	2.7	88	2.4	75	2.1	23	3.5	60	2.6
Neither	453	76.8	1,610	95.4	2,800	94.3	3,625	95.0	661	93.7	170	97.0

^aData are from the 1989 National Hospital Discharge Survey (18). Percentages are based on weighted sampling.

smaller proportion were discharged against medical advice (7.0%), were transferred to other institutions (13.7%), or died while they were in the hospital (0.2%).

Patients with mental disorders who had CT scans of the head or EEGs were transferred to other institutions at higher rates (17.3% and 18.8%, respectively) than patients with mental disorders who did not have either of these tests (13.4%). As compared with the transferred patients who did not undergo either procedure, those who had CT scans and those who had EEGs were more often sent to long-term care facilities (55.8%, 76.1%, and 67.1%, respectively). The remainder of the transferred patients with mental disorders were sent to other short-term hospitals.

The length of stay of patients with mental disorders who received CT scans of the head (mean=16.6 days, SD=26.6) and EEGs (mean=17.3 days, SD=28.8) was several days longer than that of patients with mental disorders who did not receive either test (mean=12.9 days, SD=15.4).

Discharge Diagnoses

The percentages of discharged patients with primary mental disorders in the six broad diagnostic groupings were as follows: drug- and alcohol-related disorders, 29.9%; affective disorders, 26.8%; schizophrenic disorders, 13.5%; neurotic disorders, 7.4%; organic disorders, 6.0%; and other disorders, 16.4%. Of the various groups, patients with organic disorders were the most likely to receive CT scans of the head and EEGs (table 3). The largest subgroup of patients with organic disorders (N=259) consisted of patients diagnosed as having senile and presenile organic psychotic conditions (ICD-9-CM code 290). Nearly one-quarter (23.7%) of the patients with senile or presenile organic psychotic conditions received CT scans of the head, and 10.1% received EEGs.

The number of listed discharge diagnoses was greater for patients who had received CT head scans (mean=3.91, SD=1.80) and EEGs (mean=3.64, SD=1.74) than for patients who did not undergo either procedure (mean=2.83, SD=1.65). Over two-thirds of the patients with mental disorders who received CT scans of the head or EEGs were given three or more discharge diagnoses (78.3% and 67.3%, respectively). In contrast,

only about half (49.0%) of those with mental disorders who did not undergo either procedure were given three or more discharge diagnoses.

Secondary medical diagnoses were given to only a small proportion of the patients with mental disorders (6.8%). CT scans were provided to 11.9% and EEGs to 4.8% of the patients with primary mental disorders who received secondary medical diagnoses.

Convulsions (ICD-9-CM code 780.3) and syncope (code 780.2) were the two most common secondary medical conditions of the patients with primary diagnoses of mental disorders. A high proportion of patients with these secondary medical conditions received CT scans of the head (19.2% and 39.0%, respectively) or EEGs (12.2% and 10.7%, respectively).

Hospital Characteristics

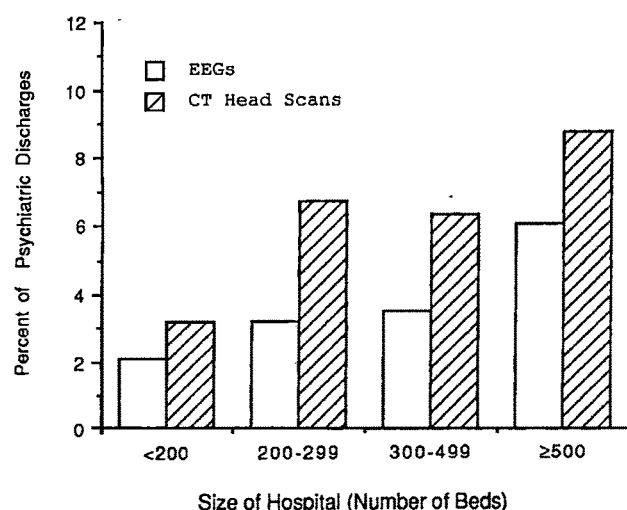
As shown in figure 1, the proportions of patients who received CT scans of the head and EEGs tended to increase with increasing hospital size. Patients with mental disorders admitted to general hospitals with 500 or more beds were more than twice as likely as patients admitted to hospitals with fewer than 200 beds to receive CT scans of the head or EEGs.

The majority of patients with mental disorders were admitted to hospitals operated by churches or other not-for-profit organizations (78.0%), rather than hospitals operated by state or local governments (14.2%) or hospitals operated on a for-profit basis (7.8%).

CT scans of the head were provided to a higher proportion of patients in government hospitals (7.6%) than patients in proprietary hospitals (6.2%) or not-for-profit hospitals (4.6%). A similar trend was observed for the frequency with which the patients with mental disorders were provided EEGs (government hospitals, 4.1%; proprietary hospitals, 3.2%; not-for-profit hospitals, 2.5%).

The proportions of patients who received CT head scans and EEGs were analyzed according to geographic region. Patients with mental disorders discharged from hospitals in the west (CT, 6.6%; EEG, 3.8%) and northeast (CT, 5.0%; EEG, 3.4%) had higher rates of testing than patients discharged from hospitals in the midwest (CT, 3.9%; EEG, 2.0%) and south (CT, 3.5%; EEG, 2.4%).

FIGURE 1. Frequency of CT Scans of the Head and EEGs Provided to Inpatients Discharged From General Hospitals With Primary Diagnoses of Mental Disorders, by Hospital Size



Relation of CT Scans of the Head and EEGs to Clinical and Institutional Variables

A logistic regression was conducted to estimate the strength of the association between the clinical and institutional variables and the provision of a CT scan of the head to patients with mental disorders. As shown in table 4, the estimated likelihood (relative risk) of receiving a CT scan of the head was substantially greater for those with a primary discharge diagnosis of an organic disorder, those with a secondary discharge diagnosis of a medical disorder, and those over the age of 65. Hospital location and hospital size had only a modest influence on the estimated likelihood of receiving a CT scan of the head.

A logistic regression was also conducted to estimate the strength of the association between the clinical and institutional variables and the provision of EEGs to patients with mental disorders. The estimated likelihood of receiving an EEG was significantly greater for patients with a primary discharge diagnosis of an organic disorder, those with a secondary diagnosis of a medical disorder, those who were in a hospital with 500 or more beds, and those treated in a hospital in the northeast or west (table 4).

DISCUSSION

The main finding to emerge from this study is that neuropsychiatric diagnostic testing is selectively utilized in the routine inpatient treatment of general hospital patients with mental disorders. The overwhelming majority of general hospital psychiatric inpatients do not receive a CT scan of the head, an EEG, or MRI of the brain.

Approximately one of every 20 (5.1%) of the patients discharged from U.S. general hospitals with a psychiat-

TABLE 4. Clinical and Institutional Factors Associated With the Provision of CT Scans of the Head and EEGs to Inpatients Discharged From General Hospitals With Primary Diagnoses of Mental Disorders^a

Variable	Odds Ratio	95% Confidence Interval
CT scans		
Primary diagnosis of organic disorder (present)	3.01	2.36-3.84
Secondary medical diagnosis (present)	2.71	2.26-3.25
Age of patient (over 65 years)	2.27	1.69-3.06
Geographic region (northeast and west)	1.57	1.32-1.86
Hospital size (500 or more beds)	1.48	1.18-1.86
Hospital ownership (government)	1.19	0.84-1.68
Source of payment (Medicare)	1.03	0.78-1.35
EEGs		
Primary diagnosis of organic disorder (present)	2.74	1.92-3.91
Secondary medical diagnosis (present)	2.14	1.71-2.68
Hospital size (500 or more beds)	1.96	1.50-2.56
Geographic region (northeast and west)	1.52	1.22-1.90
Source of payment (self-pay)	1.08	0.77-1.52
Age of patient (over 65 years)	0.98	0.71-1.36
Hospital ownership (government)	0.80	0.58-1.10

^aData are from the 1989 National Hospital Discharge Survey (18). Groups with higher likelihood of diagnostic procedures are given in parentheses.

ric diagnosis receives a CT scan of the head during the inpatient stay. This figure is in the range previously reported for psychiatric inpatients at a community mental health center (5.6%) (20) and a Veterans Administration medical center (3.6%) (8), but it is substantially lower than rates reported from a private psychiatric hospital (10%) (21) and a general hospital psychiatric consultation service (19%) (15). The estimated national rate of EEGs provided to general hospital inpatients with mental disorders (2.8%) is substantially lower than the rates previously reported from two university-affiliated general hospitals (18% and 33%) (13, 17).

Psychiatric patients who undergo neuropsychiatric diagnostic procedures have relatively complex health care needs. In comparison with patients who do not receive CT scans or EEGs, these patients tend to require longer hospitalization, suffer more commonly from comorbid medical conditions, and are more likely to be transferred to a long-term health care facility.

General hospital psychiatric patients who receive CT scans or EEGs also tend to be older than other psychiatric inpatients, and a larger proportion suffer from organic disorders. The disproportionate use of neuropsychiatric testing for older patients and those with organic disorders or comorbid medical conditions is in accord with published clinical testing guidelines (5, 13, 14). Future studies should examine the specific clinical determinants of ordering neuropsychiatric diagnostic tests for patients with organic disorders and other high-risk groups.

Beyond the finding of more testing for patients with organic disorders, the frequency of testing did not substantially vary by diagnostic group. The frequency of CT head scans for patients with schizophrenia or major affective disorders, for example, was not substantially

different from the frequency for patients with neurotic disorders. This is surprising in light of the clinical indications for CT head scanning, which include a subgroup of psychoses and affective disorders (5), and raises the possibility that CT scans may, in fact, have been underutilized for patients in these subgroups.

Patients with psychiatric diagnoses who are discharged from large hospitals are somewhat more likely than those discharged from small hospitals to have received CT scans or EEGs. Smaller general hospitals, particularly hospitals with fewer than 200 beds, may not generate sufficient clinical demand to offset the high costs of maintaining testing facilities. For hospitals without CT scanning or EEG facilities, the financial costs and clinical risks of transporting patients to hospitals with such facilities may deter test utilization.

Previous research has demonstrated that the composition of psychiatric care varies by hospital type and by the patient's source of payment. Wolff et al. (22) reported that schizophrenic patients admitted to public mental hospitals are less likely to receive a range of psychosocial treatments than schizophrenic patients admitted to private for-profit or private nonprofit psychiatric hospitals. These researchers also found that within private nonprofit psychiatric hospitals, patients with private insurance are more likely to receive some psychosocial treatments than patients without private insurance (22).

In the current study, which was limited to general hospitals, hospital ownership and the patient's source of payment did not have a significant effect on clinical practice. Once psychiatric patients have entered a general hospital, their source of payment and the hospital's type of ownership does not appear to influence the likelihood that a neurodiagnostic workup will be performed. However, the scope of this study may simply have been too narrow to detect the effects of these variables on neuropsychiatric test-ordering practices. A survey that encompasses patients in a broader range of facilities, such as private psychiatric hospitals and state mental hospitals, might have a greater chance of uncovering associations between frequency of test ordering and financial or institutional variables.

There appears to be a modest degree of regional variation in the utilization of neurodiagnostic tests for psychiatric inpatients. General hospitals in the northeast and the west exhibit higher rates of CT head scans and EEGs than hospitals in the south and midwest. The factors that cause this variation are unknown but possibly include lack of agreement about the clinical indications for testing, regional variation in the extent to which physicians base decisions on cost factors, variation in the risk or perceived risk of malpractice, variation in patients' perceptions of quality care, and variation in the extent to which testing serves to reassure patients. An understanding of the sources of regional variation in test utilization may help to promote more cost-effective care.

This study was constrained by limitations in the survey data. Perhaps most importantly, the survey does

not provide information on test results or the clinical consequences of test results. For this reason, the findings do not permit assessment of the complex relation between testing practices and patient outcome. A second limitation concerns the lack of data on admitting diagnoses. Without this information, it is not possible to enumerate patients who are admitted with psychiatric symptoms but who are discovered, during the course of hospitalization, to suffer primarily from medical disorders. Because neuropsychiatric diagnostic procedures may be relatively highly utilized for these patients, the current findings may underestimate the utilization of these procedures for patients admitted to general hospitals with psychiatric complaints.

A third limitation concerns the lack of information about the specialties of the physicians who ordered the tests. Although a majority of general hospital inpatients with primary diagnoses of mental disorders are treated in psychiatric units and therefore are presumably under the care of psychiatrists, a substantial proportion of general hospital psychiatric inpatients are treated outside psychiatric units, in so-called scatter beds (23). Nonpsychiatrist physicians commonly serve as the attending physicians for psychiatric patients in scatter beds (24). The reported patterns of test utilization reflect a summation of the test-ordering practices in unit-based and scatter bed settings.

Medical expenses are, for the most part, directly under the control of physicians (25). To curtail indiscriminate ordering of tests, policy makers have devised a series of cost-containment strategies that focus on the test-ordering practices of physicians. Some of these strategies involve overt rationing and risk-sharing plans (26).

In the area of neuropsychiatric diagnostic procedures in general hospitals, there is little evidence of widespread unnecessary testing. The provision of these tests to general hospital psychiatric inpatients is highly selective and closely related to clinical variables. Attention should now be focused on defining with greater precision the clinical indications and usefulness of such testing for psychiatric inpatients.

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Effect of Instructional Cues on Schizophrenic Patients' Performance on the Wisconsin Card Sorting Test

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***Objective:** Schizophrenic patients are particularly deficient on measures of executive functioning, notably the Wisconsin Card Sorting Test. This study was conducted to determine the efficacy of a cuing strategy in facilitating performance on this cognitive measure of the integrity of prefrontal brain structures and functioning. **Method:** Twenty-four schizophrenic inpatients and 24 demographically matched inpatients with mood disorders were administered the Wisconsin Card Sorting Test either with instructional cues at the beginning of the task or with the standard administration procedure. **Results:** There was a significant benefit of cues for the patients with affective disorders as well as for the schizophrenic patients. The schizophrenic subjects in the uncued condition maintained poor but stable performance throughout the course of the task. **Conclusions:** The study suggests that the deficit in executive functioning of schizophrenic patients may lie in the formation of concepts, not in their application.*

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Deficient cognitive functioning is a well-documented phenomenon in schizophrenia (1, 2). Recent advances in neuroradiological techniques have confirmed frontal lobe dysfunction in schizophrenia; varying degrees of hypofrontality have been found on measures of both structure and functioning—magnetic resonance imaging (MRI) and regional cerebral blood flow (3–6). While many neuropsychological studies have demonstrated generalized, nonspecific cognitive impairment in schizophrenic subjects relative to normal control subjects (7–9), other studies have shown the presence of more specific neuropsychological dysfunction in schizophrenia, namely, impairment in executive functioning (10, 11). Abilities that reflect executive functioning include planning, sequencing, concept formation, cognitive set shifting, and cognitive set maintenance (12). Executive functions are thought to be mediated primarily by the prefrontal cortex (13, 14).

The Wisconsin Card Sorting Test has been extensively used as a measure of executive functioning. Non-schizophrenic patients with focal frontal lesions per-

form poorly on this task relative to other brain-injured patients with nonfrontal lesions and normal control subjects (15–17). Performance by schizophrenic patients on the test typically reveals more perseverative errors, more perseverative responses, and fewer obtained categories in comparison to other psychiatric patients and nonpsychiatric control subjects (18–20).

Several researchers have used the Wisconsin Card Sorting Test to examine whether training can improve executive functioning performance in severely impaired schizophrenic populations. Stuss and Benson (13) modified the standard 128-card test procedure by including instructional intervention after the first 64 cards had been presented. The instructional intervention varied from the traditional administration of the test by informing the patients of the sorting principles and also informing them that the sorting principles change throughout the course of the task. Following the instructional intervention, the performance of leukotomized schizophrenic subjects did not improve with the second deck of cards, whereas the performance of the normal subjects did. Recent studies using the Stuss modification with nonleukotomized but chronic, medicated schizophrenic patients have reported a similar inability of these patients to profit from instructional feedback. Card-by-card instruction on the Wisconsin Card Sorting Test (21, 22) failed to produce an enduring learning effect after termination of instruction. Bellack et al. (23) also provided intensive instructional training on the test for a less chronic schizophrenic population and found that cuing plus a monetary incentive produced stable improvement in performance,

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TABLE 1. Demographic Characteristics and Test Scores of Schizophrenic Patients and Patients With Affective Disorders Given the Wisconsin Card Sorting Test in Cued and Uncued Conditions

Variable	Patients With Affective Disorders				Schizophrenic Patients				Analysis	
	Uncued Condition (N=11)		Cued Condition (N=13)		Uncued Condition (N=12)		Cued Condition (N=12)			
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F (df=3, 44)	p
Age (years)	37.7	9.2	40.5	9.2	37.8	6.4	35.8	6.0	1.12	n.s.
Education (years)	11.4	1.2	11.9	0.4	11.7	0.9	11.3	1.8	0.13	n.s.
WAIS-R vocabulary subtest score	9.2	3.6	10.4	3.3	8.0	2.1	9.4	2.0	1.70	n.s.
Mini-Mental State examination score	27.4	2.2	27.7	2.1	27.1	1.6	28.3	1.9	1.97	n.s.
BPRS total score	36.4	6.7	36.7	5.2	39.2	7.2	43.0	7.6	5.52	<0.05 ^a
Wisconsin Card Sorting Test										
Total errors	48.2	19.9	34.5	19.7	62.8	24.0	32.3	14.6	14.88	<0.001 ^b
Perseverative responses	31.2	21.5	19.0	11.3	53.2	35.2	17.2	9.1	14.82	<0.001 ^b
Perseverative errors	26.8	16.1	17.4	9.6	43.8	25.3	16.0	7.8	16.06	<0.001 ^b
Nonperseverative errors	21.6	10.4	17.1	10.9	18.1	12.6	16.3	8.2	1.05	n.s.
Categories obtained	4.2	3.3	6.0	3.7	3.1	2.8	5.5	2.2	3.87	n.s.

^aSignificant difference between diagnostic groups.^bSignificant difference between conditions.

while the incentive alone failed to alter performance. However, these results are unclear. The absence of a condition in which there was instructional intervention and no monetary incentive does not allow attribution of the effects of learning to cuing alone.

The present study was undertaken to examine the extent to which schizophrenic subjects, in contrast to psychiatric comparison subjects, respond to external intervention in the form of cuing to improve performance on the Wisconsin Card Sorting Test. A criticism of previous training studies with schizophrenic subjects has been the lack of nonschizophrenic psychiatric comparison subjects, who provide demographic comparability (i.e., in effects of hospitalization and presence of psychopathology). Furthermore, previous research (22, 23) initiated training after the completion of an uncued block of trials rather than at the outset, when the patients were still naive about the task. The initiation of cuing after completion of several trials may have created a cognitive schema that altered subsequent performance, thereby confounding the effects of cuing. In this study we initiated training at the beginning of the Wisconsin Card Sorting Test in an effort to evaluate the effectiveness of priming for patients who had not developed a cognitive set based on previous exposure to the test.

METHOD

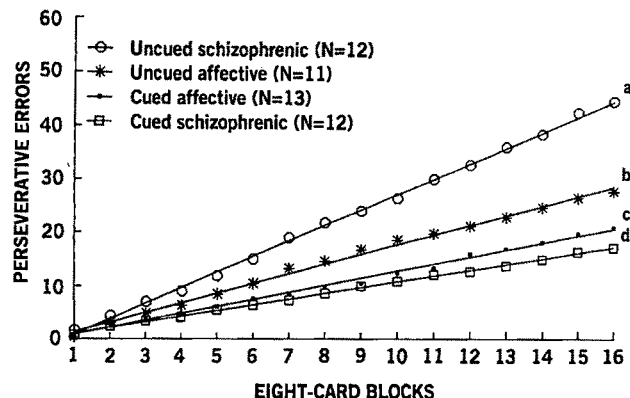
The study group consisted of 48 male patients hospitalized in the general psychiatric units at a Department of Veterans Affairs medical center. Twenty-four patients met the *DSM-III-R* criteria for schizophrenia, and 24 met the criteria for mood disorders (11 had bipolar disorder and 13 had a major depressive episode). Diagnoses were formulated on the basis of independent clinical interviews conducted by a three-member psychiatric team. Final diagnoses for the patients included

in the study required unanimous consensual validation. Exclusion criteria consisted of a history of neurological injury or illness unrelated to the psychiatric diagnosis and alcohol or drug abuse as defined by *DSM-III-R*.

The study group had a mean age of 37.9 years (SD=7.7) and a mean education level of 11.6 years (SD=1.1) (table 1). The schizophrenic patients' mean age at onset was 21.2 years (range=17–29 years). Table 1 presents demographic information and scores on the vocabulary subtest of the WAIS-R (an estimate of verbal intellectual functioning) and the Mini-Mental State examination (24). The four subgroups did not differ with respect to age, education, vocabulary, and performance on the Mini-Mental State examination. A main effect of diagnostic group was found for scores on the Brief Psychiatric Rating Scale (BPRS) (25), a measure of psychopathology. As shown in table 1, both schizophrenic subgroups had higher BPRS scores than did the patients with affective disorders. Within each diagnostic group, BPRS scores did not differ between the cued and the standard administration conditions. Furthermore, BPRS scores failed to correlate significantly with the dependent measures. The patients with schizophrenia were receiving neuroleptic and anticholinergic medications. The chlorpromazine-equivalent dose did not differ between subjects in the standard administration condition (mean=890, SD=1354) and those in the cued condition (mean=796, SD=1122).

After diagnosis and entry into the study, subjects within each diagnostic group were randomly assigned to one of the two experimental conditions: standard and cued administrations of the Wisconsin Card Sorting Test. In all conditions two identical decks of 64 response cards (26) were used. The test consists of four stimulus cards, each containing shapes that differ in terms of color, form, and number. The subject is required to sort 128 response cards according to each of three principles (color, form, and number), which are changed surreptitiously following 10 accurate sorts.

FIGURE 1. Cumulative Perseverative Errors on Eight-Card Blocks of the Wisconsin Card Sorting Test for Schizophrenic Patients and Patients With Affective Disorders in Cued and Uncued Conditions



^aR²=0.998.

^bR²=0.996.

^cR²=0.994.

^dR²=0.998.

"Perseveration" on this measure refers to an inability to recognize that a change in sorting principle (color, form, number) has been introduced, so that the patient continues to sort according to the previously correct principle despite external feedback. "Categories obtained" indicates the number of successfully learned principles out of a possible six category sorts (color, form, number, color, form, number).

In the standard administration condition, subjects were informed only of the accuracy of their responses ("correct" or "incorrect") through verbal feedback. In the cued condition, adapted from Goldberg et al. (22), subjects were informed of the three possible sorting principles at the outset. They were also informed that the principles could change at any time but were not told explicitly when the change would occur (i.e., after 10 correct sorts). These instructions were repeated for every 32 cards, a total of four times. In this study all 128 response cards were administered.

RESULTS

A 2x2 (Diagnostic Group by Administration Condition) factorial analysis of variance (ANOVA) was performed for five of the six established Wisconsin Card Sorting Test measures (26). Total correct was not studied, since the analyses would be identical to those for total errors. The dependent variables included total errors, perseverative responses, perseverative errors, non-perseverative errors, and number of categories obtained (table 1). Significant main effects for administration condition were observed for total errors and perseverative responses. Post hoc one-way ANOVAs revealed significantly better performance for the primed condition relative to the standard administration. Neither significant interactions nor main effects for diagnostic

groups were observed on these variables. No main effects or interaction effects were observed for nonperseverative errors and categories obtained.

Although no significant differences between diagnostic groups were found for perseverative errors, there was a significant main effect for instructional condition (table 1) and a Diagnosis by Instruction interaction ($F=4.00$, $df=1, 44$, $p<0.05$). Again, the performance of individuals in the cued condition was superior to that of those in the uncued condition. In addition, post hoc analyses showed that the schizophrenic subjects benefited the most from instructional cues.

Hotelling's T multivariate ANOVA with repeated measures was performed on the five Wisconsin Card Sorting Test measures between the administration of the first deck of 64 response cards and the administration of the second deck. The analyses revealed no significant difference between the subject groups in responses for the two decks ($F=0.49$, $df=18, 111$, $p>0.05$, multivariate approximation to Wilks's lambda). This suggests that performance on the test remained comparable over time for the diagnostic groups, regardless of whether they received cues. However, this analysis is not sensitive to fluctuations in performance over the course of the task.

To examine more closely the performance trends for each subject group, perseverative error scores for eight-card blocks were cumulatively totaled; these are graphically presented in figure 1. The perseverative error measure was chosen because this variable was not only sensitive to instructional set but also differentiated the patients with mood disorders from the schizophrenic patients in terms of their ability to benefit from cuing. Figure 1 illustrates the obviously inferior performance of the uncued schizophrenic subgroup. Inspection of the cumulative curves further reveals that performance did not change over the course of the task for any of the subgroups. Lines of best fit and regression coefficients (figure 1) were computed for each subgroup and statistically demonstrated no deviation from a straight line. Furthermore, matched-pairs t tests were performed on several consecutive eight-card blocks (i.e., for blocks 4, 8, and 12) to examine whether changes in performance occurred consequent to the administration of instructional cues. As expected, no significant differences between consecutive block pairs were found across all four subgroups.

DISCUSSION

This study demonstrated subjects' significant improvement in performing a task of executive functioning when they were provided with cues before beginning the task. Improved performance on the Wisconsin Card Sorting Test was found for individuals with mood disorders and individuals with schizophrenia, with the schizophrenic patients showing the greatest improvement on perseverative errors. Performance on the test in the cued and uncued conditions was unrelated to se-

verity of illness. These findings strongly contrast with those obtained by Goldberg et al. (22), who found that explicit card-by-card instruction only transiently improved performance. The differences in findings may possibly be explained by the nature of the Goldberg et al. subject group, which was composed of persons with chronic, unremitting schizophrenia. The schizophrenic group in our study was more similar to that of Bellack et al. (23), who reported significant benefits of cuing in the context of monetary incentives.

With regard to the quality of instruction, Bellack et al. (23) provided comprehensive explanations of the Wisconsin Card Sorting Test by identifying the sorting rules, providing information pertaining to change of set, and giving a card-by-card explanation of decision rules for the first five response cards. Using a less involved technique at the beginning of the task, we found a similarly strong effect of cues. Subjects in this study were informed of the sorting principles, alerted to the possibility of change without any card-by-card instruction, and provided repetition of instructions only at 32-card intervals. On the surface, this suggests that the impairment of executive functioning is not so severe as to preclude learning the test with a minimum of external intervention. However, the timing of the cues may be critical in the effectiveness of the intervention technique. Consistent with previous research in our laboratory (27), inability of schizophrenic patients to generate and shift cognitive sets occurs at the beginning of the Wisconsin Card Sorting Test and is maintained throughout the task. This may result from incorporation of an invariant, and inaccurate, internal response structure by schizophrenic patients. It appears that once a cognitive set is incorporated, schizophrenic subjects have little difficulty in maintaining that particular set. In fact, even if the formulated schema is inaccurate, schizophrenic subjects will persevere in that set despite negative response feedback. Early instructional priming may therefore provide an accurate response structure, or schema, upon which schizophrenic persons can rely in performing the task, without the need for more elaborate intervention.

If indeed performance on the Wisconsin Card Sorting Test is predicated on maintenance of an established cognitive structure, even if that schema is inaccurate, then the performance of all individuals should not vary over the course of the task. In this study, we found that the schizophrenic subjects and the subjects with affective disorders maintained stable response sets over the course of the test regardless of whether they were cued. This was clearly demonstrated by the consistency of performance in the two halves of the task and the invariant lines of best fit for the perseverative error measure (figure 1). The finding of stable performance suggests that the generation and implementation of cognitive schemas are separate functional entities. Effective performance on the Wisconsin Card Sorting Test as a measure of executive functioning relies on generation and revision of schemas as well as maintenance of those schemas. On the basis of the finding that

schizophrenic subjects are readily able to maintain schemas, one could hypothesize that the so-called neurobehavioral frontal lobe deficit in schizophrenia lies in the formulation of an accurate cognitive schema, not in its implementation. Deficits in self-monitoring and ability to regulate self-initiated behavior have theoretically been linked to frontostriatal dysfunction in schizophrenia (28, 29). The fact that the patients with affective disorders and the schizophrenic patients benefited from being cued indicates that the cuing paradigm served to provide both groups with an accurate cognitive structure with which they could effectively maintain performance, reducing the self-monitoring component of the task. These findings also suggest that memory per se is not the primary functional component underlying performance deficits of schizophrenic patients on the Wisconsin Card Sorting Test, since memory deficits would be more critical to the maintenance of a response structure than to its generation.

It remains to be seen whether performance on tasks purported to be measures of executive functioning are in fact mediated exclusively by the frontal lobes or require input from other cortical regions, such as the temporal region (30-32). The notion that multiple cognitive processes and cortical sites may be involved in performance on measures of executive functioning certainly deserves further examination.

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Physical and Sexual Abuse Histories Among Children With Borderline Personality Disorder

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***Objective:** The purpose of the study was to determine whether a history of physical or sexual abuse is more common in children with borderline personality disorder than in other children evaluated in the same outpatient psychiatric clinic. **Method:** The authors contrasted rates of abuse in 44 children diagnosed with borderline personality disorder and in 100 comparison children. **Results:** The borderline personality disorder group had a significantly greater prevalence of physical and combined physical/sexual abuse. Sexual abuse rates alone did not differ significantly between groups. **Conclusions:** The finding of greater abuse in the group with borderline personality disorder supports the hypothesis that a history of trauma is associated with the disorder.*

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Borderline personality disorder has received extensive attention in the adult and child clinical literature (1-8). Through use of *DSM-III-R* criteria, borderline personality disorder has been shown to be a valid and reliably diagnosed syndrome (9, 10) with serious, long-term emotional and behavioral consequences (11).

While diagnostic criteria have been improved, there is little consensus regarding the cause of the disorder. Psychodynamic, family, and biologic etiologies have been hypothesized (12-15). Recently, reports of a 60%-80% prevalence of childhood abuse, particularly sexual abuse, in adults with borderline personality disorder have emerged (16-18). It has been noted that the prevalence of sexual abuse differentiates patients with borderline personality disorder from comparison groups in both inpatient and outpatient psychiatric settings (17, 18). On the basis of these findings, Herman and van der Kolk (19) have hypothesized that psychological trauma, specifically abuse, plays an important role in the genesis of borderline personality disorder. They speculated that borderline personality disorder has symptomatic parallels with posttraumatic stress disorder (PTSD).

In contrast, the reports of childhood abuse in the histories of children with borderline personality disorder have been limited in nature and have tended to be confined to case reports (6, 7). Bemporad et al. (6) re-

ported a higher than average prevalence of physical abuse among their sample of 24 children with borderline personality disorder who were evaluated in an inpatient setting. Grapentine et al. (unpublished 1990 paper) noted a greater than average prevalence of sexual abuse among hospitalized adolescent girls diagnosed with borderline personality disorder. Most recently, Famularo et al. (20) have described trauma and PTSD in a sample of 19 children with borderline personality disorder.

The present study sought to determine whether a history of physical or sexual abuse is more common in children with borderline personality disorder than in other children evaluated in the same outpatient psychiatric clinic. This investigation reports on a much larger and younger group of children with borderline personality disorder than has previously appeared in the literature.

METHOD

The study was conducted in the outpatient psychiatry clinic of a tertiary care pediatric hospital. Patients were referred from a wide range of sources within and outside the hospital. The child and family member or caregiver each underwent a 1-hour diagnostic interview. Semistructured interviews were conducted by a staff psychiatrist, psychologist, social worker, or child psychiatry resident. The interview used a standard format to generate information in the following areas: current behavior and symptoms of the child; medical, educational, developmental, and family histories; and mental status examination.

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TABLE 1. DSM-III-R Criteria for Borderline Personality Disorder Adapted to Account for Developmental Differences in Childhood

Adult Criterion	Adapted Childhood Criterion	Examples
1. A pattern of unstable and intense interpersonal relationships characterized by alternation between extremes of overidealization and devaluation	A pattern of unstable and intense interpersonal relationships characterized by alternation between extremes of overidealization and devaluation and/or marked distortion of the nature of the relationship	Describing teacher as a "girlfriend," chronic inability to maintain friendships despite wish to do so
2. Impulsiveness in at least two areas that are potentially self-damaging, e.g., spending, sex, substance use, shoplifting, reckless driving, binge eating (do not include suicidal or self-mutilating behavior covered in item 5)	Impulsiveness in at least two areas that are potentially self-damaging, e.g., reckless risk taking, running away, stealing, substance abuse, sex, binge eating	Walking across railroad bridge railing, sniffing glue
3. Affective instability: marked shifts from baseline mood to depression, irritability, or anxiety, usually lasting a few hours and only rarely more than a few days	Affective instability: marked, rapid shifts from baseline mood to depression, irritability, or anxiety lasting less than a few hours and only rarely more than a few days. Episodes may include transient distortions of reality	Early-afternoon anxiety attack with persecutory delusions, followed by successful participation in soccer game in late afternoon
4. Inappropriate, intense anger or lack of control of anger, e.g., frequent displays of temper, constant anger, recurrent physical fights	Inappropriate, intense anger or lack of control of anger, e.g., frequent displays of temper, constant anger, recurrent physical fights	Easily provoked, frequent fights, threatens and attempts to throw therapist out window
5. Recurrent suicidal threats, gestures, or behavior or self-mutilating behavior	Recurrent suicidal threats, gestures, or behavior or self-mutilating or self-endangering acts	Carves boyfriend's name into arm, multiple episodes of being struck by car
6. Marked and persistent identity disturbance manifested by uncertainty about at least two of the following: self-image, sexual orientation, long-term goals or career choice, type of friends desired, preferred values	Marked and persistent disturbance in self-perception and -presentation characterized by confusion regarding two of the following: gender identity or roles, friendships, socially appropriate behaviors, school or career plans, self-image	Chronic cross-dressing, running for class president despite having no friends
7. Chronic feelings of emptiness or boredom	Chronic feelings of emptiness or boredom	Chronic complaints of boredom, unable to invest in appropriate activities
8. Frantic efforts to avoid real or imagined abandonment (do not include suicidal or self-mutilating behavior covered in item 5)	Frantic efforts to avoid or major preoccupation with real or imagined abandonment (do not include suicidal or self-mutilating behavior included in item 5)	Continual concern that therapist will not be there at next appointment, refusal to leave house while parent is at work

The interview data were reviewed at the time of the diagnostic session by an interdisciplinary team headed by the first author. A consensus diagnosis was made for all subjects according to *DSM-III* or *DSM-III-R* criteria. In cases in which patients had been diagnosed before the *DSM-III* revision, all relevant records were reviewed to determine whether patients met the *DSM-III-R* criteria. All subjects in this study maintained their initial diagnosis after this careful record review.

Subject Selection

Table 1 presents *DSM-III-R* criteria for borderline personality disorder that were adapted to account for developmental differences across childhood. From just under 2,000 consecutive subjects evaluated since 1982, all subjects who received a definite or probable diagnosis of borderline personality disorder were selected for the study. A diagnosis of definite borderline personality disorder was made when a child met at least five of the eight *DSM-III-R* criteria. A diagnosis of probable borderline personality disorder was made when a child met at least four of the criteria. The group with a probable diagnosis of borderline personality disorder was included in this study on the basis of Clarkin et al.'s finding (21) that the presence of four of the symptom crite-

ria makes the diagnosis of borderline personality disorder highly likely.

The convergent validity of the two groups was also demonstrated by using the Diagnostic Interview for Borderline Patients—Record Review (DIB-R) (22). Each record was reviewed in a blind manner and cumulative DIB-R scores were derived (23). The analysis indicated that the entire group with a definite diagnosis of borderline personality disorder and 17 of the 22 subjects with a probable diagnosis were at or above the DIB-R cutoff score of 7. Of the five remaining children in the group with a probable diagnosis, four were 1 point and the fifth subject was 2 points below the cutoff score.

A comparison group of 100 subjects was randomly selected from patients who received diagnostic evaluations in the outpatient clinic concurrently with the study group. They all underwent the same diagnostic process and clinical review as described for the study group and had a wide range of diagnoses other than borderline personality disorder.

Subjects

Of the 44 children in the group with borderline personality disorder, 32 were boys (mean age=10.8 years,

SD=3.6) and 12 were girls (mean age=12.4, SD=4.5). The families' mean Hollingshead and Redlich occupation score (24) was 4.6 (SD=1.5). The comparison group consisted of 62 boys (mean age=9.9 years, SD=4.3) and 38 girls (mean age=10.0 years, SD=3.8). Their families' mean Hollingshead and Redlich occupation score was 5.1 (SD=1.8). There were no significant differences in age, sex, or families' occupation scores for the two groups.

Assessment of Childhood Abuse

The semistructured interview data were reviewed for each subject to identify the presence or absence of childhood physical or sexual abuse histories obtained during the diagnostic assessment. It was noted that the subjects had been abused only when clear data, such as physical evidence or direct statements by the child, parent, or protective agency, were obtained. Cases in which abuse was possible or even probable but in which there was no substantiating data were not considered cases of abuse for this study. None of the subjects in cases of abuse was embedded in the complex context of custody, visitation, or divorce disputes, a context that might diminish the validity of the complaint.

RESULTS

Seventeen of the 44 children with borderline personality disorder (38.6%) and nine of the 100 clinical comparison children (9%) had an abuse history. The complex chi-square analysis revealed that the children with borderline personality disorder had a significantly greater frequency of abuse than did the comparison group ($\chi^2=25.5$, $df=3$, $p<0.001$). The contingency coefficient of 0.4 reflected this association between diagnosis and abuse status. Using the test for the significance between proportions, we found that the group with borderline personality disorder had significantly greater rates than the comparison group of both physical abuse (five versus three subjects; $z=2.1$, $p<0.05$) and combined physical/sexual abuse (seven versus no subjects; $z=4.0$, $p<0.05$). The prevalence of sexual abuse did not differ significantly between the two groups (five versus six subjects; $z=1.0$, *n.s.*).

When the group was divided according to the categories of probable and definite borderline personality disorder, no significant difference in the frequency of abuse was observed ($\chi^2=2.5$, $df=3$, *n.s.*). Similarly, when the subjects with borderline personality disorder were divided according to sex, no significant difference in frequency of abuse was noted ($\chi^2=2.4$, $df=3$, *n.s.*).

DISCUSSION

These results indicate that the prevalence of abuse is significantly greater in children diagnosed with borderline personality disorder than in other children who

come for clinical services in an outpatient psychiatric department. We have demonstrated this in a systematic manner, with a much larger and younger cohort than previously reported. The children with borderline personality disorder had significantly greater rates of both physical and combined physical and sexual abuse. However, there was no significant difference between groups in the prevalence of sexual abuse alone.

These findings correspond to studies of borderline personality disorder in adults in which a history of childhood abuse is common. However, the prevalence of abuse in the present cohort (38.6%) is less than that found in the adult studies, which report rates of between 60% and 80%. A number of possibilities may account for the lower prevalence. First, the information about abuse history was obtained from both the children and families as part of a general psychiatric evaluation in which abuse was not the referring complaint. Since abusive families tend to be secretive about these activities and children are often forced into silence (25), the lower prevalence may be a reflection of significant underreporting. Second, most (73%) of the patients with borderline personality disorder who participated in this study were male. While this is a typical pattern for school-age children referred for psychiatric disorders (26), it contrasts with the largely female samples reported in most studies of adult patients with borderline personality disorder. Given the differences in the reported prevalence of sexual abuse among female and male children (a ratio of 3:1), it is likely that the preponderance of boys in the cohort resulted in a lower overall rate of documented sexual abuse than that in an adult, predominantly female population with borderline personality disorder. Finally, it is likely that the effects of traumatic abuse have both short- and long-term sequelae for children. These effects might include the propensity to develop the disorder at a later date or the lower likelihood of improvement in the subpopulation of children with borderline personality disorder who have been abused. Both of these possibilities would increase the rate of abuse found in a cohort of adults with borderline personality disorder.

The validity of reported abuse has been the subject of professional and lay commentary for many decades. In child populations, the child's validity and credibility as a reporter have been described by several authors (27, 28). Particular controversy exists when the child is in a custody, divorce, or visitation dispute (29). None of our abused study or comparison group members were in such a dispute. The validity of the cases of abuse in the present study was substantiated by the internal and external consistency, internal detail, and interview process, as suggested by Nurcombe (27). While we felt that emotional abuse or the witnessing of abuse might play a role in the genesis of the disorder, the definitions and reporting of these were considered too subjective to be included in this study.

While a history of abuse was associated with the diagnosis of borderline personality disorder in this group of children, the study did not examine other possible

risk factors, such as parent-child interactions, comorbidity, or temperament, which might also influence psychological development and functioning. The delineation of an etiologic hypothesis that explains the interaction of important risk factors in the development of borderline personality disorder remains to be articulated and evaluated. The significant percentage of patients with borderline personality disorder who have no known abuse or biological diathesis and have been reportedly reared in supportive environments also warrants further explanation. Continued detailed and longitudinal studies are indicated in order to understand borderline personality disorder. However, what remains quite noteworthy is our finding that children with borderline personality disorder, like adults and adolescents with borderline personality disorder, have a significantly greater rate of histories of abuse than their peers. This makes the evaluation of the etiologic impact of abuse a compelling place to start and further emphasizes the parallels between borderline personality disorder and PTSD.

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Lithium-Discontinuation-Induced Refractoriness: Preliminary Observations

**Robert M. Post, M.D., Gabriele S. Leverich, M.S.W.,
Lori Altshuler, M.D., and Kirstin Mikalauskas, B.S.**

The authors used a systematic life-chart methodology to observe four patients with bipolar disorder in whom long periods (6–15 years) of effective lithium prophylaxis were followed by relapses on lithium discontinuation. Once the drug was reinstituted, it was no longer effective. The incidence, predictors, and mechanisms underlying this phenomenon all require further systematic study. The current preliminary observations suggest an additional reason for caution when lithium discontinuation in the well-maintained patient is considered.

(Am J Psychiatry 1992; 149:1727–1729)

Relapses following lithium discontinuation have helped establish its efficacy in prophylaxis (1–3). In the studies of Baastrup et al. (1) and in many subsequent studies, it appeared that almost all of the patients responded positively to reinstitution of lithium treatment. We have found, based on systematic life charting of four patients, that this positive response to reinstitution of lithium treatment may not always occur.

METHOD

The four patients were diagnosed according to *DSM-III-R* criteria as having bipolar disorder. The previous course of illness and response to medication of each patient was graphically reconstructed retrospectively and prospectively by applying systematic life-chart criteria, described elsewhere (4). Briefly, this involved assessing and charting previous episodes of depression and mania rated as reflecting mild (none), moderate (substantial), or severe (complete) functional incapacity in social or occupational roles. This was accomplished with the assistance of interviews of the patients and their family members as well as review of hospital and physicians' records. Three patients were studied before and/or after

an inpatient admission, and one was examined in an outpatient consultation setting.

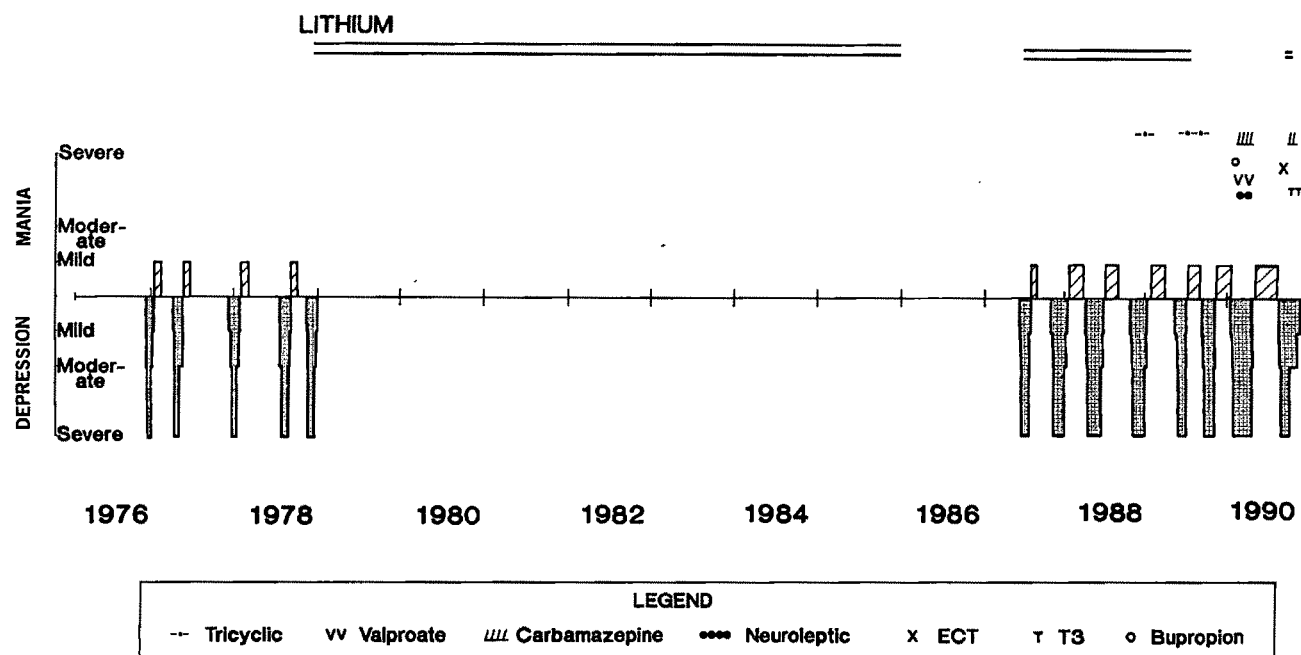
RESULTS

In all four patients, after periods of successful lithium prophylaxis ranging from 6 to 15 years, discontinuation of treatment was associated with the occurrence of relapses and the subsequent failure to respond to lithium at similar or higher doses after it was reintroduced. Multiple adjunctive treatments were also employed without success. A brief vignette of one patient's experience is summarized and illustrated in figure 1 and was typical of the experience of the other patients.

The patient whose course is shown in figure 1 was a 43-year-old married woman with five children. She experienced the onset of her illness at the age of 29, when a severe depressive episode was followed by mild hypomania lasting 5–6 weeks. After three more cycles, she was given 900 mg/day of lithium carbonate; after this she did not cycle into her usual hypomanic phase. She remained symptom free for the next 8½ years while receiving lithium maintenance treatment. Her illness reemerged 1½ years following discontinuation of lithium; she experienced an incapacitating depression, virtually identical to her initial episodes. Within days of onset of this episode, she was given 900 mg/day of lithium, but she did not respond and continued to cycle despite ongoing lithium therapy for the next 2 years.

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FIGURE 1. Treatment Refractoriness Induced by Lithium Discontinuation in a Patient With Bipolar Disorder



Augmentation of lithium with fluoxetine and alternative trials of other agents (protriptyline, bupropion, isocarboxazid, valproic acid, carbamazepine, and a course of ECT) were all unsuccessful in stopping the recurrence of the disabling depressive cycles.

The three other patients were 67-, 34-, and 52-year-old women with bipolar I disorder who experienced periods of stability lasting 5, 6, and 15 years, respectively, while receiving lithium. Each failed to re-respond once lithium treatment was reintroduced after discontinuation and the emergence of a new episode.

DISCUSSION

These four patients appear to share the common phenomenon of having a period of sustained and successful prophylactic response to lithium terminated by dose reduction or drug discontinuation. In all four patients, after their illness reappeared and lithium therapy was resumed, adequate control over their episodes was not again achieved. It is highly unlikely that the illness would have spontaneously run this course in the absence of the initial lithium-related intervention and its subsequent discontinuation. While taking lithium, all of these patients sustained remissions substantially longer than their previous well intervals. The refractory nature of the recurrences of episodes in these patients after lithium discontinuation and reinstitution suggests the possibility that biological changes occurred when these patients experienced a reemergence of episodes after lithium discontinuation and that these changes were associated with lithium nonresponsiveness. In the studies of Gelenberg et al. (5) and O'Connell et al. (6), a history

of more than three or four previous episodes was associated with a poor response to lithium, suggesting that the occurrence of an additional episode itself may have negative prognostic implications.

It is of interest that one of the patients responded to reinstitution of lithium following the first discontinuation of lithium when she was 21 years old, but not following the second discontinuation of lithium when she was 28. These data raise the possibility that, in some instances, repeated occurrences of lithium discontinuation and reemergence of episodes may be associated with the induction of lithium refractoriness. This could provide an additional basis for the occurrence of lithium refractoriness in patients with periodic non-compliance (2); i.e., repeated discontinuations might produce multiple exacerbations, ultimately generating refractoriness.

From a clinical perspective, these preliminary data, based on detailed life-chart observations, emphasize the importance of further systematic exploration of this phenomenon. In a larger series of inpatients who had had previous trials of lithium of at least 1 year's duration and who were referred to our institute because of refractory bipolar illness, nine (13.6%) of 66 patients showed clear-cut (N=7) or possible (N=2) evidence of discontinuation refractoriness. Other clinicians (J. Angst, personal communication, December 1989; A. Kukopulos, T. Hahn, and G.M. Goodwin, personal communication, June 12, 1991) have also seen patients reflecting this phenomenon of drug refractoriness following lithium discontinuation. For example, Goodwin's patient had an entirely symptom-free period of 10 years while receiving lithium. Following discontinuation of the drug and a severe depressive relapse 6

months later, the patient immediately started to take lithium again. Despite this, severe depressions (three requiring hospitalization) continued and the patient committed suicide. Such observations of the emergence of lithium refractoriness following discontinuation-related episodes may provide another reason (in addition to the risk of relapse) for conservatism when the physician and patient are considering the potential risks and benefits of a trial of lithium discontinuation.

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Side Effects and the "Blindability" of Clinical Drug Trials

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A novel, simple approach to retrospective assessment of "blindability" was applied to data on outpatients in a controlled, double-blind clinical comparison of a putative antidepressant, etoperidone, and placebo. A "blind" evaluator proved capable of discriminating between the active drug and placebo on the basis of reported side effects alone, raising questions about the true blindness of the study.

(Am J Psychiatry 1992; 149:1730-1731)

Double-blind procedures, in which drugs and placebo are coded and dispensed in identical-appearing capsules so that supposedly neither the subject nor the evaluator/treater knows which treatment is being given, have become a standard in clinical research. They are thought to remove the factor of investigator or subject bias in determining outcome. However, many clinical researchers are well aware that on the basis of side effects alone, subjects taking active drugs can often be distinguished from those taking placebo. This may be more true of psychotropic medications than of other medications such as vitamins or antibiotics because of psychotropic medications' numerous side effects.

Some previous researchers (1-4) have documented this problem and called for incorporation of procedures to assess blindness as part of the research protocol. However, this is hardly ever done or reported, perhaps because such inquiry might seem to risk invalidating results. Therefore, we devised an approach to assessment of the potential blindness of a comparative drug trial that can be applied after a study is completed, without requiring any initial planning for this in the original study methodology. Our approach was simply to provide an informed but blind evaluator with data on side effects and dosage for each subject, without reference to therapeutic effects, and to ask the evaluator to guess the treatment assignment. To avoid the aforementioned risk of appearing to invalidate results of importance to other parties, we chose to use data from a previously unpublished study of a drug that is no longer intended for marketing. Our study adds to the earlier

literature on the "unblinding" of studies by using the strategy of keeping the evaluator blind to the therapeutic effects of the treatment. Also, by using data collected years earlier, our study demonstrates the feasibility of applying this procedure to databases that are relatively remote from the current investigators.

METHOD

The data on which this study was conducted were derived from a seven-site, multicenter, double-blind three-arm comparison of two doses of etoperidone, a trazodone-like prospective antidepressant, and placebo in outpatients with major depression. Data from two sites (Belmont, Mass., and Providence, R.I.) were analyzed according to the following protocol.

Completed case report forms were reviewed by one of us (K.W.), who deleted all information pertaining to the therapeutic effects on the patients' depression and any conjectural attribution of side effects to treatment recorded by the original study assessor. This resulted in modified case report forms that described each subject in terms of that subject's initial depressive symptoms, medical history, dosage, and side effects but omitted mention of therapeutic effects during the trials. These forms were then given to the study evaluator (J.K.), who reviewed them and guessed whether each subject had received a high dose of etoperidone, a low dose of etoperidone, or placebo and made an estimate of confidence in this guess. The evaluator, a clinical pharmacist, had reviewed the investigator brochure distributed prior to the study and thus was aware of the anticipated side effects of etoperidone. In two cases in which subjects dropped out after a single evaluation while they were on the double-blind medication regimen, she declined to make any guess because of insufficient information. The data we report concern the 34 subjects, 13 in Belmont, Mass., and 21 in Providence, R.I., for whom the evaluator made a guess about treatment assignment.

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RESULTS

When the subjects taking the two dosages of etoperidone were combined into one active drug group and their data were compared with the data on the placebo group, the evaluator correctly guessed active drug assignment for 73% (N=16) of the 22 etoperidone-treated subjects and correctly guessed placebo assignment for 67% (N=8) of the 12 placebo-treated subjects. The hypothesis of independence between actual and guessed treatment assignment was rejected by use of Fisher's exact test for the four entries ($p=0.04$). Thus, the evaluator guessed more accurately than predicted by chance whether subjects received active drug or placebo; the kappa coefficient of agreement (5) was 0.38 ($SD=0.16$). She was not successful in differentiating the two dosage levels of active etoperidone ($kappa=0.03$, $SD=0.12$).

When the evaluator correctly guessed the treatment assignment, she considered herself "absolutely certain" or "quite certain" (versus the alternatives of "moderately certain" or "not certain") in the majority of cases (13 of 24, or 54%), whereas when her guesses proved incorrect, she considered herself this certain in four (40%) of 10, a nonsignificant difference suggesting limited ability to gauge correctly the reliability of her guesswork.

DISCUSSION

Those who have firsthand familiarity with conducting controlled psychopharmacology research will not be surprised that our "blind" evaluator was able to guess double-blind treatment assignment successfully on the basis of side effects alone for about three-quarters of the subjects. In fact, this is not a new finding, but it represents a potential defect in research methodology that is rarely addressed in reports of such drug trials.

Our approach is novel in that it allows an independent investigator, far removed from the original study, to retrospectively assess "blindability" of the treatment comparison under study. This suggests that numerous existing studies could be used to make a similar examination of this issue. Also, results of various studies could be combined to investigate whether the magnitude of treatment effects is greater with the drugs and the treatment comparisons that are most readily rendered "unblind" by side effects. For example, a recent meta-analysis of the efficacy of antiobsessional antidepressants suggested stronger effects for an older serotonergic antidepressant, clomipramine, with more diverse neuropharmacological effects (and side effects) than for newer antidepressants, such as sertraline and fluvoxamine, with more selective serotonergic effects and there-

fore fewer side effects (6). This result was interpreted as suggesting the importance of nonserotonergic mechanisms in antiobsessional effects, but it could merely represent the greater "unblindability" of clomipramine because of side effects.

Also, we must consider the possibility that investigators with strong biases for or against specific treatments are not fully protected by the double-blind procedure against unwittingly affecting results of their studies. The blind may be better maintained if a separate investigator assesses therapeutic effects only, without knowledge of side effects; but even then, the subject, through his or her knowledge of probable treatment assignment, may carry the effect of "unblinding" on outcome expectations. Additional methodological safeguards, such as rating symptoms before side effects, may help, but they are susceptible to the same problem. "Active" placebo treatments that mimic certain side effects may also help maintain the blind, but sometimes improvement that occurs with such treatment may raise the possibility of active psychotherapeutic effects where they were not anticipated. Of course, in some trials, depending on the severity of side effects and how different they are from typical symptoms of anxiety and depression, investigators may be unable to discriminate reliably the active drug from placebo. We would predict that in such cases, there may be a lesser magnitude of differences between drug and placebo in therapeutic effect than is observed in trials where active drug and placebo are more readily discriminated. Our investigation is not intended to call into question the validity of the large volume of controlled clinical research that has used the double-blind procedure, but it is intended to strike a cautionary note about the scientific rigor of such research and its presumed superiority to "mere" clinical observations.

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Book Forum

Nancy C. Andreasen, M.D., Ph.D., Editor

The books for this month are a holiday gift list:
books to broaden the library and the mind,
to provide pleasure and enjoyment,
to give to oneself and others.

EDITORS' NOTE: Borrowing a note from the Spirit of Christmas Past, we once again devote a portion of the holiday issue of the Book Forum to reviews of psychiatric classics. We hope that they will help to save our readers from that treacherous forgetfulness that dooms us to repeat the past.

N.C.A.
J.C.N.

The Varieties of Religious Experience: A Study in Human Nature, by William James. London, Longman, Green and Co., 1902.

A dozen years have now passed since the publication of Professor James's monumental two-volume *Principles of Psychology* (1), which introduced many of us to the phenomena of dissociation and subconscious mental processes. His review of the psychological investigation of hysterical patients by Pierre Janet and Alfred Binet in France, and of the experimental study of hypnosis and automatic writing in England by Edmund Gurney and Frederic W.H. Myers, opened up to American readers new avenues to the psychological understanding and treatment of pathological conditions such as fugue states and multiple personality disorders. In his subsequent Lowell Lectures on "Exceptional Mental States," which were delivered in 1896 but have not as yet been published, James expanded the perimeter of the subconscious mind beyond pathogenic processes to include a consideration of the subconscious origins of the phenomena of spiritualism, demon possession, witchcraft, and artistic and scientific creativity. In this broadening of the concept of the subconscious, James has been significantly influenced by the writings of Myers, who, in a series of long chapters published in the *Proceedings of the Society for Psychical Research* between 1891 and 1895 (2), had similarly defined and described what he called the "subliminal consciousness," a term that James used throughout his lectures synonymously with the word "subconscious."

As James now turns to a study of the variety of religious experiences, he enters mostly uncharted waters. A few investigators (3, 4), it is true, have published psychological studies of conversion and mysticism, and James has also had access to the large collection of autobiographical accounts of religious experiences on which Starbuck (4) based his monograph, but James's approach to the subject is thoroughly his own, marked by scientific candor and open-minded empiricism. For James, facts speak louder than theories, and a goodly proportion of his pages is taken up with the accounts by saints and sinners of religious states they have experienced through the

ages—self-reports that graphically define the terms "religious" and "mystical."

James's empirical approach is vitally necessary for an understanding of the phenomena he has chosen to study. The subjects who speak to us from these pages describe perceptions of a spiritual world that they find profoundly moving and convincingly real—states of conscious awareness that most of us have not experienced for ourselves. Indeed, James reports of himself that "my own constitution shuts me out from their enjoyment almost entirely, and I can speak of them only at second hand" (p. 370), although it should be noted that elsewhere (p. 378), despite this disclaimer, he describes having himself once had strikingly noetic mystical states of awareness in association with inhaling nitrous oxide. While most of us, therefore, will not have personally experienced any profound spiritual revelations, we may legitimately hope, under James's guidance and from a careful study of the autobiographical material he furnishes us, to *learn about* the psychological characteristics of religious states and to perceive them in their relation to other elements of psychic functioning.

Perhaps the foremost fact that the introspective reports of religious experiences reveal to us is, in James's words, "that our normal waking consciousness, rational consciousness as we call it, is but one special type of consciousness, whilst all about it . . . there lie potential forms of consciousness entirely different" (p. 378). The ordinary rational state of consciousness with which we live and operate in our practical, everyday lives is so universal and common that it seems to many people, if not the majority, to be the only worthwhile and valid state of being. At the same time, as James cogently demonstrates throughout this volume, there is a significant minority who experience occasional states of awareness of contact with a spiritual universe of being that is as real and meaningful to them as their awareness of the external world revealed to them through their senses.

Despite, however, the similarity of the noetic conviction of the reality of its contents that is common to the rational consciousness on the one hand and the religious consciousness on the other, there are significant and important differences between them. The content and imagery of rational consciousness are derived from the sensory perceptions of the external world of material objects and result from turning one's attention outward, beyond oneself. Religious consciousness, on the other hand, is an inwardly directed, nonrational, nonsensory, intuitive, and emotional awareness and perception of a non-material but vividly real presence distinct from the self. Furthermore, whereas rational consciousness can be voluntarily evoked and set in operation by focusing one's attention on sensory perceptions and actively directing the processes of logical thought and problem solving, religious consciousness,

Clearly, he has listened carefully to the speech of many patients with schizophrenia and considered how the disruptions in their ability to communicate may reflect important and basic changes in their thoughts and emotions. This has led him to identify loosening of associations as the most characteristic feature of the disorder.

Bleuler's important work contains many major contributions. First, he distinguishes the difference between fundamental and accessory symptoms. The fundamental symptoms are those which may be considered characteristic or pathognomonic of schizophrenia, while the accessory symptoms may occur in many other types of illnesses:

Certain symptoms of schizophrenia are present in every case and at every period of the illness even though, as with every other disease symptom, they must have attained a certain degree of intensity before they can be recognized with any certainty . . . For example, the peculiar association disturbance is always present, but not each and every aspect of it . . . Besides the specific, permanent or fundamental symptoms, we can find a host of other, more accessory manifestations such as delusions, hallucinations or catatonic symptoms. These may be completely lacking during certain periods, or even throughout the entire course of the disease; at other times, they alone may permanently determine the clinical picture. As far as we know, the fundamental symptoms are characteristic of schizophrenia, while the accessory symptoms may appear in other types of illness. (p. 13)

Second, in addition to making this important distinction between specific and nonspecific symptoms of schizophrenia, Bleuler has provided us with a comprehensive description of the fundamental symptoms that are characteristic of schizophrenia. These include altered simple functions, which, in addition to associative loosening, are affectivity and ambivalence. The fundamental symptoms involving compound functions include autism, attention, avolition, activity and behavior, and intellectual decline, which is probably a secondary manifestation of the other fundamental symptoms. Bleuler also provides us with a comprehensive description of various accessory symptoms, such as hallucinations, delusions, catatonic symptoms, and disturbances in memory (which are non-specific to schizophrenia).

Third, in addition to identifying which symptoms are specific and which nonspecific in schizophrenia, Bleuler has also given us a theoretical structure with which to understand the various symptoms, subdividing them into those which are primary and those which are secondary. Using the analogy of osteomalacia, he points out that the chemical and physiological processes leading to decalcification are primary and constitute the disease process, while the fragility of the bones and a tendency toward fracture is a secondary manifestation: "The primary symptoms are the necessary partial phenomena of a disease; the secondary symptoms may be absent, at least potentially, or they may change without the disease process having to change at the same time" (p. 349). Bleuler notes that we do not know with certainty what the primary symptoms of schizophrenic cerebral disease are, although he suspects that they may reside heavily in a disruption of the pathways of association and inhibition that have been established by experience.

These observations have led him to make a fourth major contribution, the renaming of dementia praecox with the word "schizophrenia," which more clearly describes the fun-

damental and primary symptoms of the disorder. These represent a fragmenting or splitting of the associative pathways within the mind (schizo = split, phenos = mind). In this context, Bleuler notes that the term "dementia praecox" is a misnomer because not all cases decline into dementia, nor do all have an onset in adolescence; Professor Kraepelin, who proposed the use of term "dementia praecox," concurs with Bleuler that there are exceptions to the characteristic typical course suggested by the name he chose. Professor Bleuler, on the other hand, also concurs with Kraepelin that patients with schizophrenia do not ordinarily have a full *restituto ad integrum*.

Bleuler's theory of the process that produces schizophrenia assumes a biological basis that is released by psychological precipitants:

Complete justice to all these factors can only be done by a concept of the disease which assumes the presence of (anatomical or chemical) disturbances of the brain: the course of the cerebral disorder is chronic, for the most part, but there are also phases of acute forward thrusts or of standstill; the disturbance of the brain determines the primary symptoms . . . As a psychic process, the disease generally, if not always, begins surreptitiously. To start with, it remains latent until an acute pathological thrust produces prominent symptoms, or until a psychic shock intensifies the secondary symptoms. (p. 463)

Bleuler notes that a long latent period may occur between the actual onset of the disease and the first manifest symptoms. In combining biological with psychological explanations for the causes and precipitants of schizophrenic symptoms, Bleuler has provided us with a framework in which we can understand both its complex causology and its complex course.

A consensus is emerging in American psychiatry that the humanely moderate ideas of Bleuler (perhaps shaped by the pluralistic, pacifistic, and democratic Swiss environment) will prevail during the last half of this century. We have learned from the past 50 years the dangers of oversimplifying, stereotyping, categorizing, or arrogantly assuming that we can predict a particular individual's experience based on our observations (misperceived or accurate) of generic group behavior, be it ethnic, nationalistic, or illness-related. In giving us the concepts of schizophrenia and the group of schizophrenias, Bleuler has given us an approach for seeing each patient as an individual person. He has instructed us to listen, feel, observe, think, and care—with appropriate recognition of our vast ignorance, as well as our modest wisdom and capacity to understand and to treat.

N.C.A.

The Ego and the Id (1923), by Sigmund Freud; translated by Joan Riviere. London, Hogarth Press and the Institute of Psychoanalysis, 1927.

The Ego and the Id was published in April of 1923. It was the culmination of what is known as Freud's metapsychological period. The slim volume introduced to the world Freud's tripartite structure of the psyche: the Ego, the Superego, and the Id. Philosophers had for centuries puzzled over the mystery of self-consciousness/consciousness of self. The Freudian trinity provided a map to the unknown regions of otherness

within the self that anyone could follow. Freud had deconstructed the self. Unfortunately, this reified explanation of mind, which solved no mystery, became the defining moment in Freud's work. Even in psychiatric circles, the Ego, the Superego, and the Id were synonymous with Freud.

The serious reader of Freud eventually discovers that there can be no definitive reading of his complicated tapestry of texts. Freud's genius flowed in many directions and was never forced through the strait gates of either/or consistency. Some of his critics, past and present, are like lawyers who want to put Freud on the witness stand and force him to answer only yes or no. Nothing gives a more distorted view of Freud's inventive and dialectic conception of the human condition. Consider how much ink has been spilled recently over Freud's supposedly "bad-faith" shift from actual sexual trauma to the imagined trauma of oedipal fantasy in the etiology of neurosis. Freud's emphasis certainly shifted, but he never denied the importance of actual sexual trauma. To hold Freud to this either/or consistency both misrepresents his theory and ignores the fact that it was Freud who made it possible for psychiatry to speak about the forbidden subject of sexual abuse, real or imagined.

Freud wrote over several decades, and he rarely looked back. Even when he did synthesize, as in *The Ego and the Id*, it was not so much an effort to reorganize his past ideas as to move on to the solution of new clinical problems. Thus, the tripartite structure provided a formula for distinguishing among schizophrenia, depression, and neurosis in Freud's subsequent papers. That application had profound influence on American psychiatry's diagnostic nosology until the dramatic departures of *DSM-III*.

The metapsychological years, of which *The Ego and the Id* is part, was a time when Freud went beyond his clinical and empirical data to build a theoretical and even speculative structure for psychoanalysis. Lacan, the great French psychoanalyst, in his cryptic but informative fashion disparaged these efforts. For him this is the "bad Freud" who made psychoanalysis into a mere "psychology." But even Freud's inner circle was skeptical about some of these writings. Helena Deutsch, years before Lacan, was critical of what she thought was Freud's departure from empiricism. The entire orthodox American school, led by Hartmann, Kris, and Lowenstein, rejected the "death instinct" and the quasi-philosophical speculations of "Beyond the Pleasure Principle" (1).

Still, if the metapsychological era was a time of abstract theorizing and off-the-wall speculation, it seemed to have gained for Freud a better clinical understanding of depression, narcissism, masochism, and paranoia. It is difficult to imagine anyone who claims a psychodynamic perspective doing without the clinical insights of these clinical-theoretical papers.

Looking back at the end of the twentieth century, I think *The Ego and the Id* must still be considered Freud's signature piece. Freud himself described this monograph as a synthesis of ideas growing out of "Beyond the Pleasure Principle." In fact, it seems to integrate ideas from all of his papers of that era and from his earliest conception of mind in the "Project." Nonetheless, the book is an unfortunate oversimplification of the great man's supple and encompassing intuitions about the particular and the universal in human nature.

Freud, despite the growing number of his disparaging critics, has met every test of a fulfilled genius. He wrote prolifically, unlike Wittgenstein; he reached a mass audience, unlike Sartre; and he kept building on his own ideas, unlike Bertrand Russell. But, despite his pretensions and those of his followers, Freud was no more a scientist than was Karl Marx. Freud reveals himself in the brief preface to *The Ego and the Id*.

Explaining the fact that he has not acknowledged the work of others in this monograph, Freud writes,

If psychoanalysis has not hitherto shown its appreciation of certain things this has never been because it overlooked their achievement or sought to deny their importance, but because it followed a particular path, which had not yet led so far. And finally when it has reached them things have a different look to it from what they have to others.

The rhetoric is vintage Freud; he used the same analogy of a mountain walk that leads to a special view in the *The Interpretation of Dreams* (2). But what he describes is not the collective enterprise of science built on the shoulders of those who went before. This is Freud, the self-confessed "conquistador" advancing the human project of self-understanding more than any other person in this century—but with the unique vision of the artist and not through the methods of science.

The Ego and the Id is if anything pseudo-science. It begins with a theme that often troubled Freud, namely, the philosophical objections to the existence of an unconscious. Freud gives his readers a few fancy philosophical arguments of his own, which he relegates to a marvelous footnote. Responding to critics who rejected the conscious, preconscious, and unconscious as only so many "gradations in intensity or clarity," Freud comes up with a *reductio ad absurdum*. He says of authors who make analogous statements, "There are varying degrees of vitality, therefore there is no such thing as death." Such statements may in a certain way have a meaning, but for practical purposes they are worthless." Freud pointed out "how this could be seen when one tried to draw a particular conclusion, 'Therefore all organisms are immortal!'"

Although he is good at it, such logic chopping is not Freud's forte. The real point was repression, the acknowledged cornerstone of Freud's theory, which explained how critical experiences were forced into the unconscious. But even as he tells his reader, "the property of being conscious or not is the last resort, our one beacon light into the darkness of depth psychology," Freud charts a course without it in the *Ego and the Id*.

Freud's first description of the conscious, preconscious, and unconscious had been drawn from immediate human experience—dreams, jokes, parapraxias, and neurotic symptoms. Here Freud instead divides the mind into hypothetical structures with particular functions: an Ego a Superego, and an Id. The latter term he took from Groddeck, who as Freud notes followed Nietzsche. He described the relation between the Ego and the Id as like the rider and his horse, an image much like Plato's centaur. More dialectical or more paradoxical than Plato, Freud took obvious pleasure in emphasizing that the highest values of humanity, along with the basest passions, came from the Id. This seems to me one of Freud's most penetrating and most neglected intuitions. The awesome power of human faith is as obscure as human desire.

If Freud's tripartite structure seems like pseudo-science today, James Strachey, Joan Riviere, and others who presided over the translation of his works into English must take some of the responsibility. As Bettelheim and others have pointed out, Freud's German was vivid and direct. The "I" and the "It" would certainly have sounded a different note than the Ego and the Id.

Chapter three of this monograph, "The Ego and the Superego," is the launching pad for modern object relations theory. Freud posits that "identification is the sole condition under which the id can give up its objects." Character is therefore

"a precipitate of abandoned object cathexes" and "contains the history of those object choices." Nothing has troubled psychiatry more than the attempt to catalog "character." However, Freud's notion suggests that all such catalogs, including his own, are beside the point. The possibility that each person's character is in some measure a record of his or her important human encounters is both profound and believable. Particularly relevant today is Freud's speculation that what was even then called "multiple personality" was the result of "different identifications seizing hold of consciousness in turn."

Along with these extraordinary speculations, Freud gives us the quantitative mumbo-jumbo of object cathexis and ego cathexis, which is even further complicated by a new theory of instinct fusion and defusion. The latter he derived from the dualism of Eros against Thanatos as set out in "Beyond the Pleasure Principle." The nineteenth-century energetic concepts in Freud have posed serious problems for twentieth-century exegetes of his work. They seem to explain everything and they therefore explain nothing. Unlike the other ideas of Freud, they constitute an impediment rather than a point of departure for contemporary understanding of the phenomena to which Freud applied them. For example, the quantity of mental energy involved explained for Freud the difference between a recurring fantasy and a delusion, or a memory and a hallucination.

The development of the energetic concepts and the distribution of quantities of energy among the Ego, Id, and Superego became a central preoccupation of the American school. Neutralized, sublimated, de-aggressivized, de-sexualized energy were incantatory terms along with "autonomous" ego functions. These concepts gradually eroded Freud's unforgiving portrait of the inherent conflicts imposed by civilization on the human savage, replacing it with a more domesticated and adaptive humankind.

If Freud's energetic concepts became a swamp for those who tried to struggle through them, his aforementioned ideas about object loss and identification presented a remarkable challenge to the Oedipus complex, the core of psychoanalysis. Most of Freud's serious readers have recognized that the female Oedipus complex was confused and confusing. Freudian feminists, Lacan, and the Kleinians have all had a go at clarifying it. But in *The Ego and the Id* Freud threw a conceptual monkey wrench into the male Oedipus complex. If the boy had to give up his erotic attachment to his mother, then according to the premise of object loss/identification the result of the Oedipus complex should be an identification with the mother, not the father. Freud, to overcome this obstacle, posits a primary identification with the father. His argument is by no means clear and it is further complicated by his insistence on the importance of bisexuality. If anything, the Oedipus complex is remystified in *The Ego and the Id*, but in its convoluted ambiguity it may reveal more about the deeper truth of gender roles and sexual object choice than in its supposed clarity.

The last chapter of the slim volume portrays "The Dependent Relationship of the Ego." It is Freud at his most brilliant and at the same time demonstrates why William James described him as a man of "fixed ideas." (The twenty-first century may yet decide that James was Freud's equal.) Freud posits three kinds of anxiety caused by the Ego's three masters: the external world, the Id, and the Superego. This would also provide the structural formula for distinguishing among psychosis, neurosis, and depression.

Paranthetically, Freud attacks the basic existential postulate—the fear of death. He insists that "to psychoanalysis . . .

death is an abstract concept with a negative content for which no conscious correlative can be found." Freud finds it "possible to regard the fear of death, like the fear of conscience, as the development of the fear of castration." The master was so bent on explaining the present by the past that he could not imagine that humanity's greatest anxiety would come from contemplation of its uncertain future.

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BIOGRAPHY

Truman, by David McCullough. New York, Simon and Schuster, 1992, 1,117 pp., \$30.00.

Harry Truman believed the White House was haunted. He wrote Bess, "I sit here in this old house and . . . listen to the ghosts walk up and down the hallway. The floors pop and the drapes move back and forth—I can just imagine old Andy and Teddy having an argument over Franklin." Once he was awakened by knocks on his bedroom door. He jumped up and put on his bathrobe, opened the door, and no one was there. "Damn place is haunted sure as shootin'," he wrote Bess.

Indeed, strange things were happening, and not just in Truman's imagination. Margaret's piano fell through the floor. Harry was told that if he sat on the presidential toilet it might fall through the floor. In truth, after nearly 150 years of neglect, the White House was about to collapse. An architect claimed he could prove mathematically that it was impossible for the house to stand.

The renovation cost six million dollars. The inside was gutted, leaving the sandstone walls standing. Under the loving supervision of Truman—historian and amateur architect—the old house was restored to resemble as closely as possible the original.

There was one addition, which hardly anyone knew about: a million-dollar bomb shelter. The military insisted on it. Truman said he would not leave Washington if there was a nuclear war, and at that time—1951—there was a "limited" war in Korea, the Soviets had the atom bomb, and a third world war was feared.

The shelter had Army cots, K rations, books, and acetylene torches to cut through the steel door if the occupants were trapped. It lacked only one necessity from Truman's standpoint: bourbon.

He had a shot of Old Grandad every morning to "get the engine going." He sipped bourbon while watching his inaugural parade, having won the 1948 election in the greatest political upset in American history. At another time, someone saw him drink five bourbons in a row, and he showed no effect. It was probably unusual for him to drink so much. In the more than 1,000 pages of this wonderful biography, he is reported to have been intoxicated only once. He was not even close to alcoholic, although he had a reputation as a drinker.

("You whiskeyguzzling, pokerplaying old buzzard," one voter wrote in an otherwise friendly letter.)

He could not have possibly drank a lot and been up at 5:00 every morning, walk for miles, work as hard as he did, maintain the remarkable physical stamina that he had, or look so young and healthy. When he became vice-president at age 60, he looked many years younger than the 62-year-old Roosevelt. Even during his retirement—which lasted 20 years—he impressed people with his youthful appearance, his bounce, his good color, the bright eyes behind the thick glasses, his good cheer, and his vitality. "Jaunty" was the word most often applied to him. He lived for 88 years and never had a serious illness until near the end. It would be imprudent to say bourbon was good for him, but apparently it did not do much harm.

This is not to suggest that drinking plays much of a role in this huge biography; it is barely mentioned. It is mentioned now because reputations are hard to shake, and this one needs to be put away. This book undoubtedly is Truman's definitive biography. It took 10 years to write, perusal of thousands of documents and letters (nearly 2,000 letters to Bess Truman alone), hundreds of interviews, long stays in Independence, Mo., and trips abroad to trace Truman's World War I experiences.

A farm boy with a high school degree, Harry Truman was an authentic hero in World War I. As captain of an artillery battery consisting of Kansas Citians, he became a hero to his men. When the war was over they kept up their friendship, became Harry's best customers when he opened a haberdashery (which failed), and promoted his career as a politician, first as county administrator and then as senator. (A man named Pendergast also helped Truman's political career; Pendergast considered Truman his honest protégé—perhaps his only one.) As long as they lived, the men in Truman's battery remained his friends. They came to Washington for his inauguration and breakfasted with Harry; he warned them not to get drunk until after the parade.

No brief review can do justice to Truman's extraordinary life and accomplishments; buy and read the book so that when it wins the National Book Award and the Pulitzer Prize, you can say you were not surprised. Here are some high points:

World War II had hardly ended before the Cold War started, with a very inexperienced Truman at the helm of the most powerful nation in the world. In rapid order came the American response to the Russian threat: the Marshall Plan, NATO, the Berlin air lift, the Korean conflict. Truman's popularity plummeted as more and more lives were lost in Korea, and firing General MacArthur led to threats of impeachment. However, when the Cold War finally ended after 45 years—without the nuclear war MacArthur and others had promoted so ardently—Truman's actions seemed eminently sensible.

Truman was a late starter. For 11 years, when others went to college or started a career, he farmed. He married his childhood sweetheart at age 35; became a U.S. Senator at age 50. He may have been a virgin when he married Bess; neither the prostitutes on 12th Street in Kansas City nor the lures of Paris seemed to undermine his Baptist scruples. Once married, Bess blushing asked the maid for new slats for the marital bed to replace several that were broken.

Truman made mistakes, and they are recorded faithfully in this book. There were scandals, but they were trivial compared with those of later administrations. Friends like Dean Acheson and Winston Churchill could not say enough admiring things about him (Churchill said he saved civilization). Even his foes, on occasion, spoke of his remarkable character, his decency, honesty, courage, and strength. He was often called the "little

man," but inside the little man—as one opponent conceded—was a blade of steel.

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Nora: The Real Life of Molly Bloom, by Brenda Maddox.
Boston, Houghton Mifflin, 1988, 368 pp., \$24.95.

Psychiatrists have long had ample reason to be fascinated by the life and work of James Joyce. His fiction explores vast reaches of the conscious and unconscious human mind, his own personality traits and struggles against adversity were remarkable, and his daughter Lucia's schizophrenia brought him into direct contact with the world of chronic mental illness. Now, with Brenda Maddox's scholarly and highly readable biography of Joyce's wife, Nora Barnacle Joyce, we have an opportunity to appreciate another Joyce and her contributions to her husband's work, while gaining a new perspective on this unusual family. For those who have read Richard Ellmann's biography *James Joyce* (1), Nora offers an excellent complement. For those who have not, it provides a fitting introduction.

Maddox begins with the thesis that Nora has been misunderstood by Joyce's critics and that her essential role in his creations has been slighted. After we read *Nora*, our view of her as the wife who "looked after" James Joyce and the woman who served as the chief model for Molly Bloom in *Ulysses* (both, of course, notable achievements) is considerably expanded.

Maddox follows an orthodox, chronological approach in telling Nora's life story. We learn of her origins in Galway, in the rural, provincial, "truly Irish" west of Ireland, her brief formal education, and early romances. She was determined to escape the strictures of her society when she moved to Dublin and took a job as a maid (at Finn's Hotel). Nora was a striking, red-haired young woman, who cut such a figure that a stranger, the nearsighted James Joyce, hailed her on the street in June 1904. They went out on a date (probably on June 16th, Bloomsday). Less than 4 months later, she eloped with him to the Continent. Maddox portrays Nora and James's difficulties—frequent moves, money trouble, the birth of two children within 3 years—clearly. We see how Nora adapted to living abroad, learning foreign languages (she could converse in German and French but favored Italian), and living with James Joyce. Joyce's peccadilloes make an impressive list: he was extravagant with money (Nora herself was no miser), had multiple phobias, had a tendency toward paranoia, and had a virulent hatred of organized religion. Nora had to conceal her faith and did not attend Mass as long as James lived. The Joyces were not legally married until 1931.

Nora also touches on Joyce's sexual practices, which ran to the masochistic and included a "cloacal obsession." Nora appears to have responded in kind to James's erotic tastes; they exchanged scatological letters when separated. These letters are explicit enough to have aroused somewhat of a storm among Joyce scholars. Rather than recreating the controversy surrounding *Ulysses'* depiction of bodily functions, readers will be best served by remembering that the letters are part of but one phase in the marriage. The biography must, of course, show what Nora did as the "woman behind the great man," but what sets the book apart is the picture of Nora as much more than servant to genius. It is made clear that Nora and James loved each other deeply and, despite James's wandering attention, faithfully. Nora was not cowed by Joyce—she was

the only one to call him Jim and to openly criticize his drinking, and she was one of the few to plainly care about him rather than his work and fame.

Maddox cites evidence that Nora was the prime inspiration not only for Molly Bloom but also for Anna Livia Plurabelle in *Finnegans Wake*, Gretta Conroy in "The Dead" (from *Dubliners*), and Bertha in the play *Exiles*. Perhaps more impressive is the thesis that Nora's spoken and written language is Molly Bloom's, and that the cadences of her speech serve as one key to the structure and sound of *Finnegans Wake*, a book she found musical and humorous. Hearing Nora's voice in *Finnegans Wake*, where one has previously only been able to detect Lucia's thought-disordered ramblings, is refreshing.

In its portrayal of the Joyces' life, *Nora* can hold the attention of any student of family dynamics. During Joyce's period of intense writing, Nora not only had to meet the needs of this highly dependent and demanding man but to raise two children. If her triumph was her support of Joyce's work, it came at the cost of providing a normal environment for her children. Maddox shows us the pain Nora felt over Lucia's severe schizophrenia and her son Giorgio's alcoholism and inability to find any sort of useful work. She felt guilt over Lucia's illness and suffered the brunt of her spectacular rages, and Nora realized the serious nature of the disorder much sooner than James did. She did not see her daughter after 1936, although she lived until 1951. Mental illness also touched the Joyce family through Giorgio's tempestuous marriage to Helen Kastor Fleischman, which ended with Helen's institutionalization for what appears to have been psychotic mania.

Nora and James's flight from Paris during the chaotic early years of World War II, Nora's attempts to encourage James to seek care for the ulcer that killed him in early 1941, and her difficulties in the years after his death are well chronicled. For me, Nora, the individual, appears traditional and innovative during a historical period that was both orthodox and revolutionary.

All in all, Brenda Maddox makes a strong case for Nora as a person worthy of respect and attention. We learn of her humor, her respect (not always acknowledged in the Joyce community) for her husband's genius, and even her ordinariness, her straightforward nature. Joyce acknowledged her as his prime inspiration, and, in his years of exile, as a "portable Ireland." In Maddox's words,

Joyce became a man in the hands of the woman who anchored him to the featherbed reality of married love, and who opened his eyes to a new artistic vision: that the most important thing in life is love That the ordinary is extraordinary is the meaning of Joyce. Nora was ordinary. That is to say, she accepted life, with its madness, drunkenness, poverty; its music, its comedy, and its sexual imperatives. Her tragedy was that Joyce never seemed to notice that their family life and her sexual appetite, which he so admired, were sacrificed on the altar of his art In every book except *A Portrait* the last words are spoken by a woman, the Nora character. (p. 380)

Nora has something for everyone interested in the complex interplay of disease and creativity, in family patterns of illnesses such as alcoholism and schizophrenia, and in the transforming power of human relationships. We come away convinced that Joyce without Nora would likely have been a pale, overly cerebral writer rather than a true celebrant of all that is human.

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Freud and Moses: The Long Journey Home, by Emanuel Rice, M.D. Albany, State University of New York Press, 1990, 250 pp., \$59.50; \$19.95 (paper).

It was almost 100 years ago that Freud began expostulating a series of hypotheses, beginning with the study of hysteria, dreams, parapraxes, and psychosexual development, that led to the establishment of psychoanalysis. The fundamental psychoanalytic theories of the unconscious, psychic determinism, and the theory of the libido were soon expanded from the analysis of individual patients to a new and exciting explanation for the most complex historical processes and cultural phenomena. Psychoanalysis was presented as a comprehensive theory of the "mind" and human behavior, and it has been a major influence for some period of time for psychiatry and psychology. This influence became particularly strong in the United States from 1910 through 1965.

With the waning of psychoanalysis and the rise of a more scientific psychiatry as well as a psychology based on diverse schools of personality theory, Freud's charisma has faded and his heroic nature have suffered in the eyes of many. However, Freud remains a major influence in academic circles that adhere to a Freudian world view that includes history, literary criticism, philosophy, and other humane (in the French sense) sciences.

Since the opening of the Freud Archives at the Library of Congress in 1980 as well as the papers of the Freud Museum in London, a number of outstanding studies of the life of Freud have shown his weaknesses in a new light. Examples include his superstitious nature, questionable medical practices with Fliess, a distortion in his presentation of the few clinical cases that formed the nexus for his developing theories, and a highly selective use of the literature (medical and otherwise) to support his hypotheses. Although he claimed that psychoanalysis was a biological science, Freud's system was closed to important psychiatric, medical, and biological developments that occurred after 1900. He held onto nineteenth-century concepts of energetics and causality and developed psychoanalysis within a closed system of adherents to his doctrines.

One major aspect of Freud's life that has been grossly neglected by his many biographers as well as by family members (including daughter Anna) has been his Jewish background, both in its religious and cultural aspects. His family has always been presented as assimilated Jews. In fact, Freud created a myth of the history of his family so that they were identified as of German rather than East European origin because of the greater esteem in which German Jews were held in Austria and Germany.

With magnificent scholarship and the decipherment of key documents, Emanuel Rice presents a most convincing argument that Freud's early life with his parents, who by no means were assimilated, was closely tied to many aspects of Judaism. Rice, a practicing psychiatrist and psychoanalyst, attended the Rabbinical School of the Jewish Theological Seminary of America and has fluency in Hebrew and Yiddish. In addition, he received help from outstanding Hebrew scholars from the Seminary, who translated Hebrew inscriptions, in particular

those of Jacob Freud in his presentation of the family Bible to Freud on his 35th birthday.

Freud and Moses consists of two basic parts. The first consists of documentary evidence of Freud's exposure to Judaism and its significance in his early development. The second part discusses Freud's return to Judaism after an alleged lifetime of scientific atheism. In the first section, Rice's central themes are supported with exciting and revealing documentary evidence of which Freud's major biographers (Jones, Clark, and Gay) have been completely oblivious. These themes include the following: 1) Freud's parents, Jacob and Amalia, come from a strictly Orthodox Jewish background, contrary to the general opinion, and they retained many of the traditional Jewish religious practices throughout their lives. 2) Jacob Freud was a Hebrew scholar who attended a Talmudical academy in his youth. 3) Freud's parents were not adherents of the Jewish Reform movement, nor were they assimilated Jews. 4) Sigmund Freud had a traditional upbringing, which he disguised in many ways throughout his early adolescence. He learned to read through the text of the family Bible as taught to him by his father and was fluent in Yiddish and Hebrew, at least in the early part of his life. 5) Freud and his immediate family disguised and rejected their Jewishness and religious background, creating a facade of a long-term assimilated status. Freud avoided the blatant issues of anti-Semitism in Vienna during his lifetime, and these issues are not discussed in any of the published notes of the Vienna Psychoanalytic Society. After his break with Breuer in 1895, Freud also rejected any identification with the Jewish community of Vienna. Breuer was an important member of this segment of Viennese life and their most outstanding physician.

The second part of the work is an expanded analysis of Freud's late and most controversial work, "Moses and Monotheism: Three Essays." Rice approaches these essays using the methods of psychoanalysis for further understanding of Freud's relationship with his father as reflected in Freud's concept of the "primal horde." This presentation merits discussion beyond this review, but its clarity and ingenuity stimulate a wealth of controversial ideas, such as the question of ontogenesis as a reflection and in turn a model for phylogenesis. In a sense, with this work Freud returned to his Jewish roots, but how psychologically internal were the determinants for this process in contrast to the national calamities of flagrant anti-Semitism in the Germanic nations after World War I?

Freud and Moses is highly recommended to all of those interested in psychoanalytic lore and to students of the life and work of Freud.

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Wilhelm II and the Germans: A Study in Leadership, by Thomas A. Kohut. New York, Oxford University Press, 1991, 320 pp., \$35.00.

In 1909 the German people were warned that "the Kaiser, about whom you are in an uproar, is your mirror image." After Germany's defeat in World War I, the minister of reconstruction, Walther Rathenau (a Jewish industrialist, soon to be assassinated), wrote that "never before had a symbolic individual [Kaiser Wilhelm II] been so completely reflected in an epoch, an epoch in an individual." Such observations about the dynamics of leadership are important; Leo Tolstoy, writing about Napoleon in *War and Peace*, raised similar questions. Do leaders determine the course of history, or are his-

torical forces responsible for bringing leaders into prominence? Now historian Thomas Kohut addresses this problem in a book about Kaiser Wilhelm II, based on his doctoral dissertation completed some 15 years ago. Drawing on his father's self psychology, Thomas Kohut characterizes Wilhelm II as a narcissistic personality, fragmented, insecure, doubt-ridden, arrogant, and grandiose, on whom Germany, a nation only recently united, projected its craving for international recognition and military power.

Born in 1859 to an English mother (Queen Victoria's daughter) and a German father (Crown Prince Friedrich of Prussia), Wilhelm sustained severe perinatal injuries: prolonged cerebral anoxia resulting in chronic hyperactivity as well as a permanently crippled left arm, which interfered with his ability to feed and dress himself and contributed to his impaired sense of self. His mother, feeling guilty and ashamed about her handicapped child, alternately overprotected and rejected him. "The idea of him remaining a cripple haunts me," she wrote to Queen Victoria, "I long to have a child with everything perfect." British and German physicians competed in attempts to rehabilitate young Wilhelm. Finally, his education was put in the hands of a stern Calvinist tutor, described by Kohut as "austere, bitter, and depressive." This man, as we see from his own description, taught Wilhelm how to ride:

Using a moral authority over [my] pupil that by now had become absolute, [I] set the weeping prince on his horse, without stirrups, and compelled him to go through the various paces. He fell off continually: every time, despite his prayers and tears, he was lifted up and set upon its back again. After weeks of torture, the difficult task was accomplished: he had got his balance. (p. 43)

Indeed, the unhappy child became an enthusiastic equestrian, loved riding in parades, and often went hunting in the royal preserves, where his servants made sure there was always plenty of game. Wilhelm's father was an ineffectual leader, overly submissive to his English wife, out of step with the prevailing mood of German patriotism, and according to Kohut an inadequate model of masculinity for his conflicted son. At age 22 Wilhelm married a German woman who was temperamentally the exact opposite of his mother, and after succeeding his father (who died of throat cancer after a brief rule) he came to depend on a coterie of male advisors who flattered, protected, and tried unsuccessfully to control him. For many years his "most intimate friendship" was with Count Philipp Eulenburg, whose homosexuality, when finally made public, led to a humiliating court scandal. Wilhelm's major political achievement, and a source of enormous pride to the Germans, was in building a huge and powerful Navy. Although it made the Kaiser seem heroic, this naval buildup intensified Germany's rivalry with England, which the Kaiser took extremely personally because of his mixed parentage. Highly sensitive to public opinion and rather lazy, he often based his policy decisions on what was printed in newspapers rather than the official documents prepared by his ministers. He ignored the advice of Germany's brilliant chancellor Otto von Bismarck, dismissed him in 1890, meddled ceaselessly in foreign affairs, and repeatedly tried to manipulate his blood relatives, namely, his cousin Tsar Nicholas of Russia and his uncle King Edward VII of England. Kohut believes that "in playing out the unresolved problems of his innermost being the Kaiser contributed to the deterioration of Anglo-German relations before the First World War" (p. 222).

Although psychiatrists can profit from reading the first part

of this book about the personal development of Kaiser Wilhelm II, the second part is difficult for anyone not thoroughly familiar with German history. Kohut gives insufficient information about political and international events to make these comprehensible for nonhistorians: the Boer War, the Samoan crisis, the Bismarck conflict, the Kruger telegram, the Moroccan crisis, "encirclement of the Reich," etc. The book is neither a biography nor a historical narrative. Ending in 1912, it leaves untold the last 29 years of the life of Wilhelm II, including the disastrous World War I, his defeat and abdication, his exile in Holland, his death in 1941, and the fate of his children. Instead, readers are given 70 pages of densely referenced footnotes.

Publication of Kohut's "study in leadership" is symptomatic of the dilemma facing psychobiographers and psychohistorians who commit themselves to exhaustive interdisciplinary research. How much and what kind of evidence is needed to make the causal connections between individuals and their social milieu seem plausible? Are psychodynamic formulations sufficient? Kohut uses them repetitively and somewhat dogmatically, but he rightly reminds us that human behavior is overdetermined. We can no longer rely on linear thinking; multiple causes lead to multiple effects, which in turn become causes. Thus, in approaching patterns as complicated as what is called leadership (in politics, science, or the arts), conscientious scholars are forced to make critical decisions between brevity—Heims's synoptic view of a collection of scientists (1), for example—versus prolixity—Richardson's multivolume study of one painter (2). Clearly, such decisions involve issues of personal taste, academic support, and publication costs.

I hope that Kohut will write a sequel to this book, giving more and deeper insights into the psychology of leadership in Germany, a country only recently reunited and already plagued with extremist tendencies that evoke memories of a deplorable historical record of intolerance and aggression.

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The Flight of the Mind: Virginia Woolf's Art and Manic-Depressive Illness, by Thomas C. Caramagno. Berkeley, University of California Press, 1992, 362 pp., \$30.00.

Despite husband Leonard's confidence that Virginia Woolf had "manic depression," biographers have demonstrated low interrater diagnostic reliability. Gordon (1) wrote that there "can be no pat conclusions about Virginia's illness" (p. 54), while Trombley (2) argued that until "concrete evidence is produced, it is irresponsible to speak of her as having been mad."

Although he is not the first biographer to put an argument for bipolar illness, Thomas Caramagno, a lecturer in English at the University of Nebraska, makes a convincing case. Equipped with the current definitive text on bipolar illness (3) and his own conscientious review, he documents classical hypomanic and melancholic features, providing a rich and complete description of the myriad manifestations of manic-depressive illness.

Many biographers have suggested that Virginia Woolf was mentally well for an extended period of time, particularly from 1916 to 1941, but Caramagno appends a mood chart that contradicts this idea. Caramagno abstracted and interpreted data from Quentin Bell's biography as well as from Virginia and Leonard's diaries (from 1913 to 1919, Leonard kept an almost daily chart of Virginia's mood state, sleeping and eating patterns, temperature, menstrual pattern, and other details). Over a 45-year period—from 1895 to 1941—she had episodes of psychotic mania and/or psychotic depression in 5, moderate or severe mood states in 22, and was euthymic for only 3 of those years.

Caramagno graphs and details a strong family history of mood disorders, involving both blood relatives (paternal grandfather, father, paternal cousin, all three siblings, and mother) as well as relatives by marriage.

After confidently addressing her diagnosis, Caramagno offers an "interdisciplinary study," reexamining Woolf's "madness and her fiction in the light of recent discoveries about the biological basis of manic-depressive illness." He gives short shrift to psychoanalytically preoccupied biographers who have interpreted all of Woolf's problems as emerging from developmental factors and who find readily available answers: "As usual in a Freudian landscape, family life is hell; why else would anyone fall ill?" Caramagno engages in deliciously selective quoting. He refers, for example, to Alma Bond's view that Woolf chose to become mentally ill to avoid growing up and that some of her lifelong difficulties "probably" resulted from her mother's having "devalued" her daughter's feces. He criticizes the view that Woolf's breakdowns were "neurotic guilt-driven responses" to a set of childhood traumata (early death of mother, sexual abuse by stepbrothers, subsequent deaths of brother, stepsister, and spiritually misanthropic father) as well as adult stressors (a pusillanimous husband who refused her children), both for its doctrinaire inflexibility in elevating theory over evidence and for its promotion of the model of the neurotic artist.

If psychoanalysis is to survive into the next century and stop "blundering into complex situations in search of a simplistic cause-effect relationship," Caramagno argues that there must be some convergence of the "soft" and "hard" sciences. While castigating those critics who fail to familiarize themselves with modern neuropsychiatry, he attempts to preempt accusations of biologism by stating that we must recognize "that our subjective lives are complicated mixtures of mind and brain, the freely chosen and the brutally imposed, the meaningful and the unintelligible."

So Caramagno does not reject the influence of developmental factors but, in offering a pluralistic "neurobiography," he suggests that Woolf handled those "emblematic events" adaptively in that she recognized a need to "develop an independent, confident, adaptive self." Fiction was for her a source of nurture and a creative mechanism for exploring pervasive themes—"mothering, madness, and the universal human need for a meaningful therapeutic mirroring of self-continuity in a world that can . . . inflict pain, loss and powerlessness."

While assertive in damning psychoanalytic views, Caramagno does not consider other reasons for some biographers minimizing or denying Woolf's "madness." Supporters of Woolf have defended her against the perceived demeaning stigma attached to such a term, while others have overreacted to the limitations of her treating psychiatrists, who have been portrayed (2) as afraid of Virginia Woolf—a liberal feminist who threatened their Victorian views (especially of a woman's role and of life requiring the imposition of black and white solutions).

Caramagno moves to a more difficult issue—seeking to explain how Woolf attempted both to explore her own bipolar symptoms in the characters she created and to integrate the consequences of her mental illness into her writing in the absence of any established formula for processing psychotic experience in literature. Although mania did quicken her imagination and depression cut into her creativity, she recognized the false perceptions of each, especially after the “shock of falling out of solipsistic mania.” She wrote best in a euthymic state where she could “reconnect mind and world” and balance “the unrestrained imagination with an external coherence,” seeking to capture a moment of being. Cassell (4) has described how sick people suffer a disconnection from their usual world and a loss of control over themselves and the world and has defined such dissolution of the social personality as illness. Most people seek strenuously to connect. Caramagno’s argument is, in effect, that Woolf sought to deal with the state of being disconnected, to define it and explore it, rather than strive for any one particular “meaning.” Further, he says that she exemplified the importance of tolerating uncertainty, confusion, multiplicity, and pointlessness because they represent the “real thing,” a message echoed of course by many contemporary writers and playwrights (e.g., Kundera and Stoppard). Woolf rejected the safety of order and went on to define the steps required to survive the loss of meaning.

Just as Woolf, in her writings, did not satisfy the reader’s need for narrative unity, Caramagno hints at an irony. Critics and biographers have sought and continue to seek definitive answers from her, from her writings (criticizing her, as an acknowledged analyst of human emotions, for refusing to sum up people) and from aspects of her life (criticizing her for not providing an explanatory statement about her suicide). Thus, they miss Woolf’s integral message—that indeterminacy is worth the risk because coherence, linearity, and closure can obscure. Caramagno reminds Woolf’s biographers of her message—that their psychological preconceptions reduce complexity to simplicity by eliminating the meaning of complexity. And that when “a psychological profile makes too much sense, something has been ignored.”

Caramagno proceeds to provide a revisionist literary analysis of five of Woolf’s novels, focusing on her illness and bipolar sense of identity. He suggests that having manic-depressive illness polarized her experience, with “oppositions . . . deconstructing . . . each other,” and that she then sought the task of integrating and fusing disparate experiences through her art, creating a sense of self that recognized the validity of the multiplicity of her experiences. She sought in her fiction “a marriage of [the manic and depressive] modes of perception, the ability to imagine wedded to a lucid recognition of reality, an epiphanic moment when her inner being and outer world co-operated with each other, each ratifying the existence and the worth of the other.” Caramagno argues that Woolf’s capacity to tolerate and deal with polarities (“bipolar cognition and syncretic vision”) emerged from her illness and right/left interhemispheric neuropsychological mechanisms. Such a view is plausible, but the frequent artistic preoccupation with polarities and dualities is not limited to those with bipolar illness.

Caramagno considers why so many successful artists have suffered from affective disorders. He suggests that manic-depressive artists not only have intensified sets of beliefs and insights (and self-confidence to risk self-disclosure in public) but also capture their unique or discordant subject-object boundaries and self-world transactions in their art, providing works that are alien to the reader’s customary ways of seeing the world. If, as is argued, interpretation is a function of iden-

tity, readers then have to set identity aside, accept the initial disturbance, and allow the literature to generate a new subjectivity within themselves. Once “occupied” by the thoughts of the author, new subject-object boundaries are drawn, discovering or reshaping aspects of the self. According to Caramagno, the manic-depressive artist has a greater capacity both to provide such an artistic effect and to provoke such reactions in the reader.

As Kay Jamison notes in an “afterword,” Caramagno gives us a “broad and compassionate look into Woolf’s life and work . . . combining the perspectives of modern psychiatry with his own background in literary criticism.” Lucid and scholarly, fresh and provocative, this is a superb book.

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Charles Ives: “My Father’s Song”: A Psychoanalytic Biography, by Stuart Feder. New Haven, Conn., Yale University Press, 1992, 368 pp., \$35.00.

Psychobiography has, until recently, been the haunt of amateurs. Typically, we (they) are trained in one of the fields, but not in the complementary one necessary to the scholarly work (if not to the occasional insight). There is some outstanding work, such as that of Erikson and Steven Marcus, but Freud’s work on Leonardo (1) is seriously marred by his mistranslation of the primary datum, and Slater and Meyers’ understanding of Handel (2) was led astray by their reliance on secondary and tertiary sources. The problem of specialized skills is further compounded when the field of study involves specific technical knowledge, such as music.

Charles Ives, that most American of American composers, requires a biographer with just such multiple and overlapping skills, and he has found them in Stuart Feder, a psychiatrist, psychoanalyst, musician, and, above all, a scholar. Feder begins his book with a skillful evocation of mid-nineteenth century Danbury, Conn., and the generations of Iveses, a historian’s accumulation of multiple illuminating details. The composer’s father, George, despite or perhaps because of his family’s banking and merchant background, was a trained musician, a Civil War Army bandmaster, and, by the time of his early death, a failed professional musician and a failed businessman. However, he remained a hero to his son Charles. Feder gives us the details of Charles Ives’s growing up, his education at Yale, his stumbling into the insurance business, his marriage, and his physical and mental deterioration, but the focus is on Ives the composer, identified with as well as remembering and memorializing his father.

A characteristic of Ives’s music is its autobiographical reference. This takes many forms: quoted tunes, crossing sounds mimicking the “noise” of two bands playing different marches, imitations of his father’s musical and sound experi-

ments as well as the words of his songs and his comments on the manuscripts. All of these, along with Ives's own writings, are used to build a convincing argument for a continuing fantasy of continued musical collaboration with his father. What is remarkable is that this is done with a refreshing absence of psychoanalytic jargon and reference. (There is reference to only a single paper by Freud.) Similarly, Feder is also able to communicate meaningfully about the musical devices Ives used and at times invented, such as particular chords and dissonances, polytonality and polyrhythmicity, without resort to highly technical language. Although conflict clearly played a role in the nature of the musical product, the compositions transcend that portion of their origin and reach out to the universals that underlie our response to great art. Ives's music is an "aesthetic crystallization of . . . nostalgia," his own personal affectively colored remembering as well as our sense of our own personal and historical past.

Curiously, although understandable in a book intended for a broad audience, Feder does not make any psychiatric diagnoses. However, the data are presented. My own differential would include spelling disability and perhaps other learning difficulties early in life, manic-depressive disease, and postinfluenzal encephalitic organic brain disease. The lattermost may well account for Ives's increasing irritability, shaky handwriting, and other difficulties. The now undeterminable diagnoses are not central, however. More important, we are provided with a rich view of both man and composer, of mental function and mental product, and of how one led to the other by shaping the passage of sound and silence through time. *Charles Ives: "My Father's Song"* is an appropriate model for how to do psychobiography or, for that matter, biography right: use primary sources, recognize the distortions present even in primary data, be cautious in interpretation, and insist on overlapping confirming data. Ober (3) recently pointed out that each teller of a tale reshapes it to fit his or her own needs and that we must trust the tale and not the teller. Feder tells the story whole; I believe the real Ives lives in this book. It is also a delight to read, cleanly and elegantly written.

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THE HUMAN EXPERIENCE

How It Feels to Fight for Your Life, by Jill Krentz. Boston, Little, Brown and Co., 1989, 144 pp., \$15.95.

This is a handsome book from an award-winning author-photographer and a distinguished publishing house. It is the result of a series of interviews with children who have or are facing serious illness.

It does not claim to be scientific. In fact, the author sought a biased sample: "I traveled around the country to find and

listen to very special kids." The intention was to produce an inspirational, instructional work. Children were sought "who were dealing with their adversity in ways that would inspire and instruct other sick kids and the adults who love and work with them."

Fourteen portraits are presented of children and adolescents aged 7-16 years with illnesses ranging from congenital heart disease requiring open heart surgery, through cancer and a host of other diseases and traumas, to childhood diabetes.

Is there anything the profession can learn from these children? Joseph Buck, Elizabeth Bonwich, and Alisha Weissman, although grateful to their doctors, find them to be somewhat uncommunicative and draw greater support from other health care professionals and other patients. Three children mention contact with psychiatrists, but only one, Spencer Gray, finds this to be beneficial. A number of the children have strong religious beliefs, but Stuart Ugelow says he "lost any hope of believing in religion . . . If there is a mighty and powerful creator who controls the world he wouldn't let things like this happen." Two are very critical of healthy people who smoke tobacco. Elizabeth Bonwich suggests that "one of the requirements for a medical degree should be to have had a serious illness."

The book is not written or intended for consumption by professional behavioral scientists. Therefore, to judge it by such standards would be unfair. Nevertheless, no account of a primary emotional disorder is offered, and this is an omission. Loss of family, incest, childhood depression, and suicide are painful experiences that could have been included. There is, however, mention of the symptoms of posttraumatic stress disorder in the account of a burned patient and a suggestion of the same in an adolescent with traumatic paraplegia.

As expected from this accomplished artist, the black and white graphics are outstanding. Severely ill children and their families need immediate, interactional relationships that address their own specific problems, so this book may not be an "inspirational" work that can stand alone. But it may help.

The value of this book is the insight it provides into the way certain children and adolescents have dealt and continue to deal successfully with massive adversity. It is an object lesson to all middle-aged adults. It has a place in all school libraries, where it will inform, encourage, and inspire healthy children.

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Before Their Time: Four Generations of Teenage Mothers, by Joelle Sander. New York, Harcourt Brace Jovanovich, 1991, 190 pp., \$19.95; \$9.95 (paper).

Last year, I received a Christmas present in July from Dr. Andreasen, a book to review that touched an area I was particularly interested in: ethics. This year, my gift was a book dealing with teenage pregnancy. I expected to find a dry statistical treatise, replete with a number of interesting but soon to be forgotten pages. Instead, I was a spellbound reader of the personal story of four women: 20-year-old Leticia Johnson; her 39-year-old mother, Denise Benjamin; her 63-year-old grandmother, Rena Wilson; and her 83-year-old great-grandmother, Louise Eaton.

Over a period of 4 years, these women told the story of their lives, their pregnancies, and their experiences as young mothers to Joelle Sander, a writer, researcher, and therapist. The voices of these women who became teenage mothers are amplified by an introduction written by Dr. Robert Coles, an oral

historian, who reminds us that "it is hard for us, no matter our good will, to quite fathom the circumstances of those who live at a great remove from us—their lives, their assumptions and expectations so different from ours." He is, indeed, right. Although my daily practice brings me in contact with impoverished black and white teenage mothers, this longitudinal slice of the lives of four black women made their stories much more real. Through the ebb and flow of their memories, their thoughts, and their feelings and through their voices, I learned not only about their early pregnancies but also about the struggles that have scarred their lives and the progressive emotional and moral disintegration of their families. These families, which started out as hard-working, upwardly mobile, and responsible, have steadily disintegrated because of the severe stress attendant to poverty, unemployment, and skin color. Like Dr. Coles and Ms. Sander, I was moved as I read of the experience of these families and the social and personal tragedies that these women experienced and continue to experience.

Ms. Sander takes to task our national priorities, policy, and programs. Each woman whose life is described in this book has complained about the economic, psychological, and social struggles she faced as a child and continues to face. Each has complained about the unresponsiveness of federal, state, and local governments that claim to provide aid and assistance. Ms. Sander makes recommendations that we have heard before. She first looks at the familial dynamics that led to all of these women's pregnancies—loss of a father through abandonment or death, loss of a mother through neglect or depression, and loss of a responsible peer group and the premature substitution of a male, any male, and a baby, any baby, to offset vulnerability. Ms. Sander makes recommendations with regard to services and programs that encourage young people to be sexually responsible. She makes it clear that total abstinence is not the answer; it will not work: "Although only five percent of teenage girls and 17 percent of teenage boys report having intercourse by their 15th birthday, 44 percent of girls and 64 percent of boys report being sexually active by the time they reach 18. More alarming is the fact that only 40 percent of teenagers report using contraception sometimes." Although the availability of contraception and contraceptive services is vital in protection from pregnancy, contraception is only the beginning. Young people need clear and comprehensive sex education; they need to have the options of adoption and legal abortion. Young people who choose to keep their children need services to help them cope—prenatal care, health care for themselves and their children, opportunities to finish their education (including on-site child care), psychiatric and psychological counseling, and parenting skills classes that are accessible. They also need fathers who are interested and available parents—for themselves and for their children. Ms. Sander suggests a need for a school system that stresses not only sound academic skills but work training and work opportunities, a school system that has links to industry and decent non-dead-end jobs.

For the most part, Ms. Sander's suggestions focus on outside interventions rather than psychological changes. It is clear that it is difficult, if not impossible, to effect change when one leaves for school in the morning hungry and returns from school to an empty refrigerator with no promise that there will be food tomorrow.

1990 census data from the Children's Defense Fund, a non-profit group based in Washington, D.C., documented the extraordinarily high levels of child poverty in my home town of Detroit, where 46.6% of children under the age of 18 (about 138,000 children) are in poverty, 6.7% more than in 1979,

and 52.4% of children under age 6 (about 56,450 children) are in poverty. The fact that one out of two children in Detroit lives in poverty reflects the impact on children of the disappearance of factory jobs in once-thriving automobile cities, and this is an underestimate. These children go hungry at the end of the month when food stamps run out, have limited access to health care, suffer physical and sexual abuse and neglect, drop out of school, and become teenage mothers. Abstinence is not a solution for these children; neither is simple access to contraception.

In 1989, the federal government spent \$21.5 billion to support families started by teenagers. What will they spend in 1995 and in the year 2000? Now, in the 1990s, nothing short of a national resolve is needed to significantly reduce the tragic circumstances that these four women have suffered. We must face the challenge and change national priorities. I thank Dr. Andreasen for helping me to think about the real meaning of the holiday season.

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Words I Never Thought to Speak: Stories of Life in the Wake of Suicide, by Victoria Alexander. New York, Lexington Books (Macmillan), 1991, 238 pp., \$22.95.

When I arrived home one evening, I found this book waiting for me. I had plans for the evening, but as I flipped through the book, I realized that it had to be read immediately. The stories of survivors (Victoria Alexander defines "survivor" as one who has experienced the loss of someone close through suicide) are compelling. This book was conceived by a woman who experienced the loss of someone close through suicide. In her eloquent introduction, she describes the difficult process of writing her book—listening to the experience of others and writing about her own; the times she stopped the process because it was too painful.

The book is divided into four chapters. The first deals with the secrecy and silence surrounding suicide and the need for survivors to tell their stories, to find language that can communicate their feelings. Alexander describes the regions of grief and some of the concomitant feelings that survivors may have, such as relief or anger, as well as the overwhelming confusion. It is in the subsequent chapters, however, that these concepts are best described. The strength of the book lies in the personal stories.

The following chapters are loosely based on a time sequence of mourning—"At the End/At the Beginning," "The Midland," and "Then and Now." As the author points out, the book can be read in different ways—reading each chapter in any order or following one person's narrative through time. I chose the latter because I wanted the continuity of each person's storytelling.

The survivors describe the initial shock and disbelief (one woman, whose mother had threatened and/or attempted suicide at least twice a year during her lifetime, thought that her mother had been murdered when she finally "succeeded") and the minute details (a coffee cup, a look, a hand squeeze) that can take on an eerie significance in the mind of a survivor. The stories confirm the universality of some of these responses. One mother ruminates as she reanalyzes the situation, "What if I had noticed, had insisted . . ."

The stories also describe the realignment of relationships once a family member is gone (a woman who becomes the only child after her brother dies, a woman who must work on

her relationship with her lover's children after her lover dies), the anniversary rituals, and the reemergence of overwhelming feelings during holidays and other milestones.

All the individuals who have shared themselves in this book seem to have a positive outlook on their own lives, although a suicide of someone close can bring the thought of suicide closer, too. It is no longer an abstract idea.

Although the people in this book do not represent all "walks of life"—all appear at least college-educated and many have graduate degrees—the stories reveal the universality of the confusion, feelings, and healing that take place after the suicide of someone close. The stories also describe more than the experience of a suicide survivor. Anyone living with someone who has a mental illness (in many of the stories, the person who committed suicide had a history of previous attempts as well as unstable and unpredictable behavior) or anyone who has suffered a death of someone close can read these stories and find feelings and thoughts that resonate with their own. It is a book that all mental health professionals should read and be able to recommend to their colleagues and patients.

MICHELLE KIM LEFF, M.D.
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Stronger Than Death: When Suicide Touches Your Life, by Sue Chance. New York, W.W. Norton & Co., 1992, 176 pp., \$19.95.

The death of a child violates the natural order. Children should bury parents, not the other way around; the fear of a child's death is arguably a parent's worst nightmare. When a child dies and this death also happens to be a suicide, the aftermath may be unendurable for survivors. Depression, post-traumatic stress disorder, and psychosomatic illness commonly strike suicide survivors, clouding their lives for years. Unfortunately for some, their entire life is plagued by dysphoric symptoms. Emotionally, these survivors are among the walking wounded, unmistakably experiencing the dispirited sense of self common among those who have suffered the purposeful death of a loved one.

On November 16, 1984, Dr. Chance's son, Jim, committed suicide by gunshot. He was 25 years old and her only child; he was also bright, sensitive, and silently depressed. Disheartened about his future, he could not imagine that life still expected something of him. His self-perceived flaws proved fatal, while his mother viewed these same flaws as insignificant compared with the rest of him.

Psychiatrists may already be familiar with the author from her regularly featured column in *Psychiatric Times*. Dr. Chance's column usually addresses relationship issues in a tone that is chatty and much like a letter to friends. This new book is different. It is a tightly written, well-crafted work with sharp focus and brutal honesty. The writing style is vivid and direct. Undoubtedly, Dr. Chance loved her son, and her writing, in part, brings him back. It is remindful of the lines John Gunther wrote in *Death Be Not Proud* about his son, who died of a brain tumor: "I want to make some part of him come alive, if only in the feeble light of words" (1). The strength in *Stronger Than Death* is love: the life-giving dynamic that points to creativity, growth, and adaptivity. In the wake of tragedy, Dr. Chance's suffering shows that love can make one better, not bitter.

Years ago, I learned that recommending books to friends, colleagues, and patients is a tricky business, even when the

text is carefully selected and well-intentioned. Despite this, I know of no other book that so poignantly addresses the aftermath of a completed suicide for survivors. There seems to be scant professional or lay literature on the impact of suicide on friends and family. Victoria Alexander's *Words I Never Thought to Speak* (2), written for the popular press, comes to mind as an exception. The intent of *Stronger Than Death* is not to cite the reasons and myriad misperceptions that lead a person toward suicide, themes which are rehearsed widely in psychiatric writing. Instead, the author explores the seemingly bottomless emotional anguish endured by survivors, and she hopes to help others by sharing her pain and knowledge. She properly recognizes that although a suicide victim's blood is on that person's hands only, the act of suicide places a skeleton in other people's closets, overshadowing their lives with tears, loneliness, guilt, and obsessive rumination. The message in *Stronger Than Death* echoes Viktor Frankl's credo: "In a word, each man is questioned by life; and he can only answer to life by answering for his own life; to life he can only respond by being responsible" (3). For survivors, the therapy of recovery starts with turning to others to endure the unendurable, and slowly, with communication, the wound that feels so private begins to be understood within a greater story.

The author kept a journal for 9 months following her son's death. She shares selected passages, interspersing them throughout the book and thus enriching the text with graphic documentation of the slow and almost imperceptible pace to recovering and getting on with life.

Psychiatric writing concerning suicide concentrates almost exclusively on epidemiology, diagnoses, risk management, and prevention. In this regard, Sue Chance, as a psychiatrist, has broken new ground by writing a book that examines the grave repercussions the act of suicide unchains among the living. This book is intended for a broad audience, with specific importance for all primary care physicians, mental health professionals, those contemplating suicide, and survivors who have suffered the suicide of a friend or loved one. Yearly, an estimated 200,000 people in the United States are added to the ranks of suicide survivors, and this book offers practical treatment approaches to promote their healing.

Stronger Than Death is a plainspoken and important book for clinical psychiatrists. When next browsing in a bookstore, pick it up and glance at the first paragraph, a powerful prelude to an inspiring story.

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Child Prodigies and Exceptional Early Achievement, by John Radford. New York, Free Press, 1990, 255 pp., \$22.95.

Curly Sue, Little Man Tate, and Kevin (who gracefully vanquished the bad guys when he was left home alone) attest to the fact that this is an era of prodigious moppets. This book tills this familiar ground with diligence and, delivering even

more than its title promises, delves into the ever-fascinating relationship between exceptional capability and accomplishment. Can precocity be measured? How specific or general is it? What are the conditions that bring it about? Can it be fostered, and if so, how? To his credit, John Radford conducts a lucid and engaging tour of this tricky territory with its political and ethical minefields—territory that is strewn with the wreckage of scientific skullduggery, parental chicanery, and media hype that feeds on public credulity.

Radford's sources range widely from the professional literature to the popular press. He reviews both the classic studies of Galton, Lombroso, and their ilk and the more recent and more systematic work of Terman, Watson, Rutter, and Gardner. There are gossip and fascinating life history data on such famous prodigies as John Stuart Mill, William James Sidis, and Norbert Wiener. More journalistic accounts describe the lives of the Quiz Kids, child movie stars, feral children, and idiots savants. A broad swath of precocity and accomplishment is covered—in music, science, mathematics, literature, chess, competitive sports and games, and even spirituality and leadership. Radford also takes up the perennial concern with fostering and enhancing high accomplishment. He reminds us that concentrating special educational methods on small children to develop their intellectual potential is not solely the invention of post-Sputnik America. Such attempts go back to Ulysses, who engaged Mentor to teach and guide his son Telemachus, to James Mill, whose careful regimen fostered John Stuart Mill's sober genius, and to many other less prominent parents through the ages. We learn that Japan, the Soviet Union, and Britain have all been hospitable at one time or another to bold experiments in expanding children's capabilities.

Radford appears to be baffled by one important finding in all the studies: that youthful capability, however measured, and actual adult achievement are not closely correlated. He seems aware that something is missing in his understanding of the issue—a factor that he sometimes refers to as motivation, or the ability to apply oneself to the task. If he had read chapter 14 of *Manic-Depressive Illness* by Goodwin and Jamison (1), he might have divined a clue to the missing factor and thereby enriched the book. These authors clearly document that the manic-depressive diathesis is highly correlated with extraordinary achievement. The energy, rush of ideas, and associative exuberance of mania, when harnessed and channeled, propel talent into the orbit of high achievement. Any of us who practice within or near great universities can attest first-hand to the contribution of hypomania to creativity and intellectual accomplishment.

Child Prodigies and Exceptional Early Achievement offers the reader a lively, comprehensive survey of a thoroughly engaging field. It does so without pretending to offer new solutions to many of the familiar riddles, foremost among which is the mysterious concatenation of biological, social, and psychological conditions that have produced such individuals throughout recorded history.

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MILES F. SHORE, M.D.
Boston, Mass.

THE GENERATIVE MIND

The Lopsided Ape: The Evolution of the Generative Mind, by Michael C. Corballis. New York, Oxford University Press, 1991, 351 pp., \$24.95.

Perhaps there is no more blissful state for the academic than being obsessed with a theory that is not only consuming but begins to explain everything. Whether one inflicts these obsessions on the world or keeps them as a private delight is always the problem. Dr. Corballis has chosen to share his obsession with us. What emerges is a most interesting book about the left hemisphere of the brain, its language functions, and how it has evolved over time. This is an interesting book that charts the evolutionary development, not only of language but of brain function as well.

The book begins with a major question. The first chapter is entitled, "Are Humans Unique?" This is succeeded by seven chapters, each of which can stand by itself, covering the topics of human evolution, the development of bipedalism (or the implications of learning to walk and having one's hands free), human handedness, human language, the evolution of language, language and the brain, and praxis and the left brain. Each of these chapters is an excellent review of the literature in its area, although as reviews they all have the usual problem of being too superficial for the expert and too detailed, perhaps, for the layman. In general, however, they are quite readable. Each chapter is written so that it can stand alone, and, as such, each would be a nice *Scientific American* essay.

The last three chapters, "The Generative Mind," "The Duality of the Brain," and "The Plastic Brain," are the crux of Dr. Corballis' argument, and argument it is, because very few data are presented. Basically, he postulates that there is a generative assembling device that is based on vocabulary and located in the left hemisphere. It is this ability to generate language and images that distinguishes human beings, in great part, from the rest of the animal world. He notes, "It is the basis of a discontinuity that is at least of the order of that which distinguishes animals that fly from those that do not. The proof of this is that a Generative Assembly Device (GAD) did eventually permit us to fly in airplanes, helicopters, and space capsules, and only as a particular case of a very general power that this bestows upon us" (p. 311).

His conclusions are very theoretical, but Corballis' book is a gold mine of many interesting tidbits and facts about evolution and handedness, and while it will not change anyone's research endeavors, it certainly is an extremely interesting book to read about the relationship of man to the rest of the animal kingdom. He discusses the implications of handedness and how left-handed people have been treated throughout the ages, even reporting that there is some evidence from flint tools from 150,000–200,000 years ago indicating that their makers were right-handed.

GARY J. TUCKER, M.D.
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LITERATURE

A Dream of Mind: Poems, by C.K. Williams. New York, Farrar, Straus and Giroux, 1992, 100 pp., \$16.00.

"I couldn't put it down" is a phrase not often associated with a volume of poetry. This book is an exception. C.K. Wil-

liams, who won the 1988 National Book Critics Circle award, is one of the nation's most gifted poets. He writes about the themes that tend to interest psychiatrists—sex, love, jealousy, anger, aging, disease, and dying. Like many psychiatrists, he is also interested in the workings of the mind, turning his attention inward and creating a sort of poetic metapsychology of dreams, meditation, prayer, and abstractions about mental life. His genius is most striking when he observes and communicates the moment, the incident, the image of a person. For example, in "When," he describes a dying man,

he wanted out of the business, out of the miserable game, and he told whoever would listen, whenever they'd listen, wife, family, friends, that he'd do it himself but how could he, without someone to help, unable to walk as he was, get out of bed or up from the toilet himself?

In "Harm," he sees that a homeless vagrant relieves himself in the street,

and that a slender adolescent girl from down the block happened by right then, and looked, and looked away, and looked at me, and looked away again, and made me want to say to her, because I imagined what she must have felt, It's not like this, really it's not this, but she was gone, so I could think, But isn't it like this, isn't this just what it is?

In "Child Psychology," Williams speaks of latency and libido, of oedipal adventures and the return of the repressed, when

we were going somewhere and without telling him I took my father's keys and went outside to wait. House, car, office keys: how proud I was to be the keeper of that weighty, consequential mass. I stood there, tossing it from hand to hand, then, like my father, high into the air. And then I missed, and saw it fall, onto the narrow grating of a storm sewer, and then in.

In "The Cautionary" (my favorite poem in the volume), which was first published in *The Times Literary Supplement*, Williams writes about a man and his attractive, somewhat younger wife:

he decides that it's not he himself, as himself, his wife desires, but that she simply *desires*. He comes to think he's incidental to this desire, which is general, unspecific, without object, almost, in its intensity and heat, without a subject: she herself seems secondary to it, as though the real project of her throaty, heaving passion was to melt her mindlessly away.

In "Helen," Paris says of the dying Helen,

The next night her cough was worse, with a harsher texture, the spasms came more rapidly, and they'd end with a deep, complicated emptying, like the whining flattening of a bagpipe. The whole event seemed to need more labor: each cough sounded more futile than the last,

as though the effort she'd made and the time lost making it had added to the burden of illness.

Williams is introspective and self-reflective. In "She, Though," narrated by a writer, he speaks of the dedication of an artist:

That dedication, or obsession, or semblance of obsession, counted for much in those days. For most of us it was all we had, struggling through our perplexed, interminable apprenticeships. We were trying to create identities as makers and as thinkers, and that entailed so much.

When he writes about people or events, this self-awareness leads to a double consciousness of what was and of what the poet saw and felt and thought about what was. We have access to a vivid representation of the world and at the same time share a privileged participation in his personal view of it. This self-awareness works less well when it is directed only inward. A third of this book is occupied by the cycle of 16 poems providing the title for the volume. The cycle starts with "The Method":

A dream of method first, in which mind is malleable, its products as revisable as sentences, in which I'll be able to extract and then illuminate the themes of being as I never have. I'm intrigued—how not be?—but I soon realize that though so much flexibility is tempting—whole zones of consciousness wouldn't only be reflected or referred to, but embodied, as themselves.

Later, in "Vocations," he explains,

they can be considered in a way that implies consequence, what I come to call the dream's "meaning." Although I can't quite specify how this ostensible meaning differs from the sum of its states, it holds an allure, *solutions* are implied, so I keep winding the dream's filaments onto its core. The problem is that trying to make the recalcitrant segments of the dream cohere is distracting.

In "The Gap," he adds,

So often and with such cruel fascination I have dreamed the implacable void that contains dream. The space there, the silence, the scrawl of trajectories tracked, traced, and let go.

He also says, in "The Fear,"

In my dream of unspecific anxiety, nothing is what it should be, nothing acts as it should; everything shifts, shudders, won't hold still long enough for me to name or constrain it. The fear comes with no premonition, no flicker in the daily surges and currents of dream.

I read these impatiently, eager to get back to narratives with plots and characters. Williams' gift of language is immense and apparent, but without the content of real people and concrete events, his view of mind and mental life failed to hold me.

Of course, poetry is the music of language as much as the

meaning, and Williams is a virtuoso of words. His style is quite distinctive; his lines are said to be the longest of any poet writing today. This permits, or perhaps demands, that he include all of the possibilities inherent in each thought, each moment. He turns to runs of words in which the same consonant is used repeatedly when he wants to carry us with him through an image and then shifts to short, almost clipped syllables when he wants us to pause and consider. For example, in my favorite, "The Cautionary," we have "a man who's married," who broods "fretfully on her faithfulness," and observes with a "degree of detachment" until the flow is disrupted as "it dawns on him in a shocking and oddly exciting insight."

The impact of this is subliminal: one must study closely to discern how Williams achieves his effects, but the impact is nonetheless powerful. Others who attempt to use language to communicate ideas with emotional impact might well consider their use of language as carefully.

Williams deserves a wide audience. He is an important poet and a first-rate psychologist as well.

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When Nietzsche Wept: A Novel of Obsession, by Irvin D. Yalom. New York, Basic Books, 1992, 306 pp., \$20.00.

This book is an artful mixture of fiction and fact. A prominent, middle-aged, Viennese physician (Josef Breuer) goes to Venice in 1882 hoping to subdue his guilty desire for sexual intimacy with a patient he has been treating with massage and psychotherapy (Bertha Pappenheim). He meets a seductive feminist (Lou Salomé) who persuades him to treat an ex-lover suffering from migraine and "despair" (Friedrich Nietzsche). Reluctantly, Breuer agrees to meet Nietzsche in Vienna, but not before we learn about the doctor's busy life there, his devotion to patients, his world-weary depressiveness, his flirtation with his office nurse, his ambivalence toward his wife and family, his fear of death, and his self-loathing. A stabilizing influence seems to be his friendship with a young neurologist ("Sig" Freud), who enjoys taking hot baths and copious meals with Breuer's family and discussing interesting cases with him.

Nietzsche's philosophizing and reluctance to disclose any personal problems proves highly frustrating for Breuer. They engage in long dialogues about truth that seem labored and beside the point in view of Nietzsche's concern regarding whether he will become a chronic invalid. Freud suggests to Breuer that "stress" might be a causal factor in migraine and that psychotherapy could prove useful (one of several ahistorical episodes in this book—the concept of stress did not enter medical thinking until nearly three-quarters of a century later) (1). After a few nonproductive sessions, Nietzsche collapses because of a severe migraine attack and nearly dies. Breuer then decides to try an unorthodox approach. He hospitalizes the patient under an assumed name and suggests that they exchange roles. Now Nietzsche is the doctor and Breuer the patient. Breuer reveals some weird dreams (faucets dripping insects, machine parts, and odious slime), which Nietzsche tries to interpret using techniques like free association, guided imagery, and behavior therapy, but nothing helps. While strolling through a cemetery Nietzsche and Breuer come upon Breuer's family tomb, and Nietzsche notices that Breuer's mother's name was Bertha. Breuer grudgingly acknowledges that there may indeed be a future for the "talking treatment"

and for "Angst doctors" who are trained to understand what symptoms mean. His obsessive desire for Bertha suddenly becomes clear:

The more blatantly she idolized *me*, the more I imbued her with power. She was the anodyne for all my anguish. Her merest glance cured my loneliness. She gave my life purpose and significance. Her simple smile anointed me as desirable, granted me absolution for all bestial impulses. A strange love: we each bask in the radiance of one another's magic. (p. 231)

Nietzsche too makes a discovery—that there can be therapeutic value in "applied philosophy."

We must look to *meaning*. The symptom is but a messenger carrying the news that *angst* is erupting from the innermost realm! Deep concerns about infinitude, the death of God, isolation, purpose, freedom . . . now break their bonds and bang at the doors and windows of the mind. (p. 232)

The novel reaches its climax when Breuer reveals (to Freud, not Nietzsche) his hedonistic fantasies, and Nietzsche, weeping, acknowledges a basic need for human contact. Patient and doctor embrace; Nietzsche returns to Switzerland to write his famous book about Zarathustra.

The author, Irvin Yalom, is a professor of psychiatry at Stanford University, an expert in group psychotherapy, and a persuasive writer. Using the format of a semihistorical novel allows him to express much wisdom and many doubts about the efficacy of psychotherapy and to explore sensitive issues regarding the doctor-patient relationship without having to worry about problems of confidentiality. But it exposes him to another risk—that of promoting historical inaccuracy. There undoubtedly will be readers of this book who believe it was Nietzsche and not Freud who catalyzed the discovery of psychoanalysis, just as there are those who believe Mozart was killed by Salieri after seeing Peter Shaffer's influential *Amadeus*. In a concluding "author's note," Yalom tries to sift fact from fancy by explaining who the characters in his novel actually were and that Breuer and Nietzsche never met. But in doing so he manages to perpetuate another myth: "In 1882, psychotherapy had not yet been born" (p. 305). In fact, not only has psychological healing been known for centuries, but there was widespread interest in moral treatment, persuasion, hypnosis, and other kinds of "talking cures" (2) before Breuer and Freud, especially in the nineteenth century.

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PETER F. OSTWALD, M.D.
San Francisco, Calif.

Suttree (1979), by Cormac McCarthy. New York, Vintage Contemporaries, 1986, 471 pp., \$6.95 (paper).

Although classics in literature are often cited by psychiatrists for their penetrating insights into human activities and

emotions—Tolstoy, Dostoevsky, Sophocles, Shakespeare, Faulkner, and Joyce come to mind—we often fail to realize that contemporary works may attain such stature. Such books are at times hidden among the massive outpouring from the publishers, and do not become widely known. Cormac McCarthy's *Suttree* is such a novel, existing in some obscurity, but deserving of our closest attention and elevation into the canon of classics. It is a work I came to love years ago, and find myself returning to time and again.

Cormac McCarthy was born in 1933, served in the Air Force and attended the University of Tennessee. He has apparently lived most of his life in and around Knoxville and in west Texas. This is practically all the information that he allowed to become known about himself, before a *New York Times Magazine* interview (April 19, 1992). As psychiatric readers and reviewers, we cannot indulge in our sport of speculation about the writer's intrapsychic processes and their impact on his work. The novel must stand alone.

Suttree is the fourth of Mr. McCarthy's six published novels, and his masterpiece in terms of style and scope. His most recent work, *All the Pretty Horses* (1), has received excellent reviews and is accessible enough to win him the wide audience he deserves. If *Suttree* gains our attention through this process, we will all be enriched. McCarthy has been classified with the Southern Gothic writers, but he also has a place in the naturalistic tradition of the underclass with authors such as Jean Genet, Nelson Algren, Charles Bukowski, and William Kennedy.

Suttree is set in Knoxville, Tenn., and the surrounding country in the early 1950s. It covers an undetermined period in the life of (presumably) relatively young man, Cornelius Suttree, who has forsaken his genteel family to fish for a living and live among the homeless, alcoholic, and criminal elements of his community.

Although the content of *Suttree* can often be depressing, its language is rich and powerful. The novel is essentially a prose poem, humorous, colloquial, archaic, descriptive, and lyrical in turn. Echoes of Faulkner, Thomas Wolfe, and even Joyce can be heard, though McCarthy has his own voice. This superb writing is hard to convey in fragments; it is really necessary to read the entire book and experience its astonishing scope. However, the following passage from a brief idyll of Cornelius Suttree's can convey something of the book's delightful texture:

The willows at the far shore cut from the night a prospect of distant mountains dark against a paler sky. Halfmoon incandescent in her black galactic keyway, the heavens locked and wheeling. A sole star to the north pale and constant, the old wanderer's beacon burning like a molten spike that tethered fast the Small Bear to the turning firmament. He closed his eyes and opened them and looked again. He was struck by the fidelity of the earth he inhabited and he bore it sudden love.

As we follow the protagonist through his activities, almost every event reflects mortality and the weight of a reality unmoved by human desires or plans. We are often uncomfortable with this awareness. When Irvin Yalom wrote in *Existential Psychotherapy* (2) that "the clinician rarely encounters death anxiety in its stark form," he was speaking about many of our clinical experiences, but not about *Suttree*:

Recurrences of dreams he'd had in the mountains came and went and the second night he woke from un-

easy sleep and lay in the world alone. A dark hand had scooped the spirit from his breast and a cold wind circled in the hollow there. He sat up. Even the community of the dead had disbanded into ashes, those shapes wheeling in the earth's crust through a nameless ether no more men than were the ruins of any other thing once living. Suttree felt the terror coming through the walls. He was seized with a thing he'd never known, a sudden understanding of the mathematical certainty of death.

In this book, we are made to see what is often hidden from us in our life and work.

Cornelius Suttree appears to lead a life without the ordinary defensive processes people use to cope with the overwhelmingly difficult awareness of death. Before we are more than a few pages into *Suttree*, we see a suicide victim hauled from the river with a grappling hook, while Cornelius notices "with a feeling he could not name that the dead man's watch was still running." We soon learn that Suttree is an identical twin whose co-twin was stillborn, and that even as a child he "had already begun to sicken at the slow seeping of life." The intensity of his exposure to death rarely abates in 471 pages, although by the end he may have come to some kind of rapprochement. Suttree must attend his young son's funeral, is present at the violent death of several people close to him, and is near death himself on three occasions. After the last, a long, delirious bout with typhoid fever, he returns to his houseboat to encounter a corpse in his bed. So he lives, and while not triumphing over death, he may transcend it in a way, becoming less haunted and preoccupied. Such, at least, is the view of *Suttree*'s major literary critic, Vereen Bell (3). To the reader, the novel transcends through a paradox at its heart—even the most mortal scenes are written in language that is intensely alive. Sometimes the power of the world and all the life outside ourselves sickens us, but often in *Suttree* we are simply amazed at its vigor.

Suttree is certainly not a mere pathography—though alcoholism, anxiety, various personality disorders, dementia, delirium, and dysthymia are portrayed, and we may come to feel more empathy with the next unwashed, homeless patient we encounter in the emergency room. Diagnostic labels could be given to Suttree and, beyond them, we can see death anxiety as a major determinant of his behavior. Ultimately, however, explanatory systems fail and we encounter the mystery of another, separate person. While frustrating, this uncertainty can be a fruitful source of speculation, a creative force. A work of fiction that offers a nonclinical, nonexplanatory perspective on life reminds us not to settle for the easy answers in psychotherapy, pharmacotherapy, or research. *Suttree* does this, as well as taking up residence within the reader.

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Vox, by Nicholson Baker. New York, Random House, 1992, 156 pp., \$15.00.

In this age of 1-900 late-night promises, Nicholson Baker puts forth the real thing. His one-sitting novel, *Vox*, is a compelling exposure to sex and intimacy in a modern culture. Three thousand miles apart, a man and woman find the other's voice through a phone number in an adult newspaper advertisement. They talk for 4 hours about their experiences and methods of gratification, by no means all sexual. They are gentle with each other's fantasies, appreciative of creativity and humor. Their revelations clearly delight the teller as much as they do the recipient—he discloses, then she, then he, and so on; by the end, the giving and receiving are completely balanced.

Abby and Jim are the responsive, eloquent pair who place sensuousness on an even higher plane than they do sexuality. Indeed, it is difficult to imagine how they would make use of their keen perceptivity and playfulness if, after dialing 2-v-o-x at \$1.90 per minute, either was randomly connected to the type of person who seeks anonymous verbal sex. But, just who would that be anyway? The socially defective and frustrated or the erotically disposed, who craves immediate voice-to-ear closeness sealed in a fiber optic vacuum? Abby and Jim, as members of the latter group, certainly get their money's worth; they invite vulnerability by telling each other their most lovingly crafted fantasies and intensely personal experiences. Paradoxically, it may be the fleeting encounter with a stranger, rather than the sustained relationship with a partner, that is most hospitable to this type of exchange. With only a single sensory modality between them, trust develops quickly. The attunement is so perfect that, ultimately, they become afraid their connection will be destroyed if they talk again, let alone meet.

I suppose one could view all this as a commentary on the contemporary strategies of finding a mate. Or on the afflictions of the 1990s, such as AIDS. Or the hard-driving-profes-

sional's-stunted-capacity-for-intimacy. Or compulsive self-reliance in the midst of the disintegrating family. Are these at the core of the characters' dialogue, which emphasizes synchronous masturbation rather than intercourse? After all, one senses that they have left a trail of incomplete relationships behind them. Still, there is little desperation, little embarrassment. Any self-consciousness, of which personal advertisements typically reek, evaporates early in their conversation. If one feels a bit sorry for these two it is not because they are lonely people seeking salvation (they don't seem so) but, rather, because it is so rare that two people can understand the other's pleasure and language this deeply, and they may never meet or talk again.

Vox probably takes as long to read as the phone conversation lasts but is decidedly cheaper at 10 cents a page than the per-minute telephone rate. The book is ensconced in a stark black paper jacket that shows signs of violation within moments of purchasing. Is it a mere coincidence that the black paper picks up and subsequently announces every molecule of innocent moisture on one's hands? Is this some clever play on the concept of voyeurism?

Nicholson Baker has a stunning capacity to make the mundane vibrant. An earlier book, *The Mezzanine* (1), is also an exercise in compressed time; it has a single character whose one-way trip up an escalator serves as the stimulus for an exhilarating cascade of associations. In *Vox*, Baker transports his characters to eventual climax. For the reader who appreciates textured prose and creative verbal intercourse as well, gratification is imminent.

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Reprints of Book Forum reviews are not available.

Letters to the Editor

Fluoxetine and Suicidal Preoccupation

SIR: Martin H. Teicher, M.D., and associates (1) reported the emergence of intense suicidal preoccupation during fluoxetine treatment, with an estimated incidence of 1.3%–7.5%. We reviewed all patients who received fluoxetine from the outpatient pharmacy at a Veterans Administration hospital during the period of April 1989 to April 1991. Policy dictated that patients must have failed more traditional pharmacotherapy or have another clear indication for use of fluoxetine. Fluoxetine was prescribed for 255 patients. Of these, six patients did not take the fluoxetine. Of the remaining 249, follow-up was obtained for 206, or 82%. One hundred thirty-six patients were studied retrospectively, and 71 patients were studied prospectively (beginning August 1990). Information was provided by the treating physician.

Physicians reported suicide history and any change in suicidal or homicidal ideation during treatment. In those few cases where an increase was reported, we spoke to the physician directly to obtain details. Patients included 183 men and 23 women, mean age=46 years (SD=1). Major depression was diagnosed in 159 patients (77%). Other diagnoses included 76 patients with substance abuse disorder (37%), eight with bipolar affective disorder, 25 with panic disorder (12%), 33 with dysthymic disorder (16%), eight with obsessive-compulsive disorder, 14 with borderline personality disorder, and 28 patients with other personality disorders (14%). In our patient population, 111 (54%) had a history of suicidal ideation and 45 (22%) had a history of suicide attempts.

Mean dose of fluoxetine was 30 mg/day (range=5–120 mg/day). Thirty percent of patients treated showed no real improvement taking fluoxetine. Two patients, one with schizophrenia complicated by depression and one with major depression, posttraumatic stress disorder (PTSD), borderline personality, and active alcohol abuse, became agitated and had a recurrence of suicidal ideation of the same quality as had occurred previously. One patient with borderline personality disorder had a similar recurrence of homicidal ideation. None of these patients had fluoxetine discontinued because of these thoughts, but none of them responded to fluoxetine, either. Of the remaining patients, 28% had a decrease in suicidal ideation, the others showed no change. However, not one of the patients showed the emergence of the intense, obsessive, violent suicidal preoccupation described by Dr. Teicher and associates (1).

Our patient population of more than 200 patients failed to demonstrate even a single case of intense suicidal preoccupation, despite the incidence of 1.3%–7.5% predicted by Dr. Teicher and associates. These results agree with those presented elsewhere (2). Fava et al. suggest that this phenomenon may be more rare than originally suggested or that it may be restricted to a subpopulation of those treated with fluoxetine. The patients in our study were a population with chronic psychiatric problems, treatment resistance, high comorbidity, and history of suicidal ideation and attempts. However, we had fewer women and fewer patients with borderline personality than most outpatient populations. Further studies of

large patient populations are necessary to confirm that de novo intense suicidal ideations are a side effect of fluoxetine.

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Fluoxetine in Depersonalization Disorder

SIR: Symptoms of depersonalization may occur in a wide range of psychiatric disorders (1). Depersonalization disorder, however, with depersonalization symptoms in the absence of more common comorbid conditions, is an apparently rare syndrome (2). While depersonalization symptoms may respond to pharmacotherapies targeting various psychotic, affective, and anxiety disorders, little conclusive information exists regarding the psychopharmacologic treatment of depersonalization disorder (2, 3). Hollander et al. (3) reported on the successful use of serotonin reuptake blockers in six of eight cases of depersonalization. We report a case of depersonalization disorder that responded favorably to fluoxetine.

Mr. A, a 73-year-old man, complained that for many years he had experienced a "sense of unreality" and felt as though he were "in a fog." He reported feeling like a "disembodied intelligence" and described "seeing things as shapes and abstractions without emotional content." He described a sense of "dullness," with "colors not sharp" and reality seeming "less than full." He stated that "the world seems like a photographic negative." When he recalled events in his life, he felt as though he was "not in them." Eight years in psychodynamic psychotherapy had promoted useful insight but had not led to sustained symptomatic relief. Past history included probable panic attacks during adolescence without subsequent recurrence or persistent fear of having a panic attack. He admitted to mild, chronic anxiety, which he felt was related to his experience of reality as "dimmed." Mr. A denied depressed mood or anhedonia, and his symptoms fell short of *DSM-III-R* criteria for any specific anxiety or mood disorder, or other comorbid axis I diagnosis. For occasional insomnia he had taken flurazepam, 15 mg h.s., or trazodone, 25 mg h.s. His medical history included hypothyroidism and asthmatic bronchitis, for which he took levothyroxine, 0.25 mg/day, and intermittently theophylline, 200 mg b.i.d., respectively. The presenting psychiatric symptoms antedated these medi-

cal problems, and Mr. A experienced no exacerbation of the symptoms in relation to medication use.

Mr. A began treatment with buspirone, 5 mg/day, which increased to 5 mg b.i.d. after 1 week. After 2 weeks taking buspirone he discontinued it, believing it ineffective and becoming more anxious. Fluoxetine, 20 mg/day, was then prescribed. Four weeks later he described a clearing of the "fog," with reduction in associated anxiety. Three months later he reported feeling much better, and 8 months after initiation of treatment he continued to experience moderate improvement in depersonalization symptoms and marked reduction in associated anxiety. Asked to describe the improvement in his depersonalization symptoms, Mr. A replied that when he reflected on his life events, it seemed that he was "more in them."

This case lends support to the observation of Hollander et al. (3) that serotonin reuptake inhibitors may be effective for some patients with depersonalization disorder. Interestingly, although our patient experienced an overall reduction of his presenting symptoms following treatment with fluoxetine, he emphasized remission of anxiety to which he had admitted only secondarily on initial presentation. One might speculate that this patient's depersonalization disorder represented a subclinical anxiety disorder that was subjectively unmasked in the course of successful pharmacologic treatment. While this notion contrasts with the suggestion that panic is a lesser form of depersonalization (4), it is consistent with the concept of depersonalization as a dissociative disorder, in which dissociation serves a protective function to prevent the emergence of overwhelming anxiety.

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Adverse Vascular Effects Associated With Fluoxetine

SIR: As briefly reviewed in the letter of J.A. Yaryura-Tobias, M.D., and associates (1) adverse vascular effects have previously been reported to be associated with the withdrawal of fluoxetine (Dista Products Company, *Fluoxetine Hydrochloride*, *Adverse Reactions*, 1989). These researchers subsequently reported eight cases of bleeding in patients diagnosed with obsessive-compulsive disorder and treated with fluoxetine. We would like to report symptoms in a single patient possibly associated with fluoxetine. The symptoms were recurrent over two trials of medication. No such symptoms were ever noted prior to fluoxetine treatment.

Mr. A, a 38-year-old man, was involved in psychotherapy with a diagnosis of both dysthymia and associated char-

acterologic dysfunction, including symptoms consistent with the diagnosis of obsessive-compulsive disorder. Fluoxetine treatment was initiated at a dose of 20 mg/day and increased during the second month to 40 mg/day. The patient developed inflammation and apparent bruising of the great and neighboring two toes of both feet. At the same time, the patient developed sporadic spontaneous epistaxis at a frequency of approximately two times per week, which resolved with the application of external pressure.

Because of an absence of therapeutic response and reticence on the part of the patient to increase dosage, fluoxetine treatment was discontinued after 3 months. Psychotherapy continued without additional biological treatment. The physical symptoms remitted concomitantly. During this first fluoxetine trial, no association between these symptoms and fluoxetine was hypothesized.

Fluoxetine treatment was reinitiated after approximately 8 months at a dose of 20 mg/day, increasing to 40 mg/day and then 60 mg/day over a 2-month period. Spontaneous epistaxis and inflammation and bruising of the patient's toes with infection of the toes reappeared. On this occasion, a dermatologic consultation was sought and clavulanic acid, 250 mg t.i.d., was prescribed. The infection resolved over 7 days. However, inflammation and bruising consistent with vascular spasm phenomena (acrocyanosis) remained. The epistaxis, at a frequency of approximately two times per week, again was controlled with externally applied pressure.

Further medical evaluation, including hematologic and thyroid studies, indicated no abnormalities. Laboratory tests revealed a platelet count of 195,000/mm³, a WBC count of 3600/mm³, and a hemoglobin level of 14.1 g/dl. Fluoxetine dosage was increased to 80 mg/day. With no therapeutic effect noted after 30 days, the fluoxetine was tapered over a 4-week period. Epistaxis as well as aforementioned bruising and inflammation diminished with reduction in dosage and disappeared when fluoxetine was reduced to 20 mg/day.

We believe that this case report supports the concerns of other authors (2-4) regarding potentially significant bleeding problems associated with fluoxetine treatment.

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Phenelzine Treatment of Depression in Parkinson's Disease

SIR: We present the case of a patient treated with the monoamine oxidase inhibitor (MAOI) phenelzine and L-dopa-carbidopa combination who showed marked improvement in both the Parkinson's disease and depression.

Mr. A, a 72-year-old man, was admitted to a psychiatric unit. He had a 30-year history of progressive Parkinson's disease and a 2-year history of treatment-resistant agitated depression. He had been unresponsive to antidepressants (amitriptyline, nortriptyline, protriptyline, desipramine, fluoxetine, tranylcypromine, and trazodone) and anti-anxiety agents (alprazolam, lorazepam, and clonazepam). Neurological examination revealed resting tremors of all extremities, shuffling, unsteady gait, and stooped posture. Primitive reflexes were also present. Neuropsychological testing revealed moderate to severe deficits in orientation, memory, attention, and abstract thinking. Magnetic resonance imaging (MRI) revealed mild atrophy and increased signal in the periventricular white matter. The diagnosis of Parkinson's disease with dementia was made. Mental status examination was conducted. His mood was depressed and extremely anxious, but he denied suicidal plans. He was not hallucinating or delusional. He was uncooperative and required a great deal of nursing staff assistance.

Initially Mr. A was treated with L-dopa-carbidopa combination, 25/100 mg t.i.d., for depression and metoclopramide, 10 mg t.i.d., for hiatal hernia. Over the next 5 weeks, his medications were adjusted to a final regimen of phenelzine, 15 mg h.s., L-dopa-carbidopa combination, 25/100 mg b.i.d., and sucralfate (phenelzine was associated with gastrointestinal upset). By the seventh week he was no longer depressed and was able to attend independently to himself. He improved enough to ambulate around the hospital grounds without assistance. Because of family problems, Mr. A was discharged to a nursing home.

There has been a recent significant trend in the treatment of Parkinson's disease to use the selective MAO-B inhibitor selegiline to slow the progression of the disease and enhance the efficacy of L-dopa (1). The combination of nonspecific MAOIs and L-dopa has been avoided due to the reported risk of serious side effects, specifically hypertensive crisis. However, the L-dopa-carbidopa combination, containing a peripheral dopa decarboxylase inhibitor, may allow safer use of MAOIs. Therefore, use of a nonspecific MAOI may be a fortuitous agent to treat both Parkinson's disease and depression. The patient described here had longstanding Parkinson's disease and a history of tricyclic-resistant depression. This patient's mood disorder was consistent with atypical depression (2), a form of depression common among patients with Parkinson's disease. MAOIs are useful in treating tricyclic-resistant depression (3), atypical depression (4), and depression associated with dementia (3). Treatment with phenelzine and L-dopa-carbidopa combination resulted in substantial reduction of our patient's depression and movement disorder. Mr. A's clinical improvement may be related to the mechanism of action of phenelzine. Acting as both an MAO-A and an MAO-B inhibitor, phenelzine may have beneficial effects on both depression and movement disorders related to insufficient norepinephrine, serotonin, and dopamine. This case suggests that the combination of low-dose phenelzine and L-dopa-carbidopa combination can be a safe alternative drug regimen for the pharmacological treatment of depression in patients with Parkinson's disease.

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Antidepressants, Panic Disorder, and PTSD

SIR: The phenomenology of posttraumatic stress disorder (PTSD) flashbacks and panic attacks is similar (1), and flashbacks and panic attacks often coexist (2, 3). However, antidepressants are effective for the treatment of panic disorder (4) and relatively ineffective for PTSD. While both imipramine and phenelzine significantly improved PTSD symptoms in a study by Frank et al. (5), in other controlled studies amitriptyline showed only modest results with respect to PTSD symptoms (3), and desipramine did not improve anxiety or other PTSD symptoms (6). We report a case in which desipramine blocked recurrent panic attacks but did not prevent the development of PTSD.

Ms. A, 21 years old, had a 2-year history of panic disorder. Four of her five siblings also had panic attacks. Her unprovoked panic attacks were marked by anxiety, shortness of breath, palpitations, chest discomfort, dizziness, trembling, and fears of dying, losing control, and going crazy. Her attacks occurred daily. She became panic free when treated with imipramine and later with desipramine, after imipramine was discontinued due to side effects. After 1 year of desipramine treatment with doses between 200 and 250 mg/day, she became pregnant and discontinued medication. She then became severely symptomatic. Ms. A was restarted on desipramine and again became symptom free. After another year of treatment, she was abducted and raped. While still panic free she developed PTSD, with typical symptoms that included psychic numbing, nightmares, startle response, hypervigilance, avoidance of situations that reminded her of the abduction, and intrusive thoughts of the rape. She received counseling for PTSD and continued desipramine treatment, still panic free. Her PTSD symptoms gradually subsided over 2 years; however, her panic attacks recurred 3 years after the trauma when tricyclic antidepressants were discontinued. She responded to treatment with fluoxetine.

Desipramine successfully blocked panic attacks in our patient before, during, and after a traumatic event but did not prevent the development of PTSD. While only a single case, this unusual set of circumstances suggests that panic attacks and PTSD do not share a common diathesis.

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Taking Chronic Fatigue Syndrome Seriously

SIR: The recent article by Susan E. Abbey, M.D., and Paul E. Garfinkel, M.D. (1), on neurasthenia and chronic fatigue syndrome contains many statements suggesting that chronic fatigue syndrome is a trivial illness and not worthy of serious medical or psychiatric consideration. Stating that chronic fatigue syndrome is an "illness behavior" molded by social pressures does a great disservice by dismissing the suffering of patients with this illness because of a lack of understanding of its etiology. The role of the physician should be to attempt to alleviate pain and suffering rather than to belittle it.

I feel that the article is unfair and selective in its treatment of the topic by reworking today's knowledge of chronic fatigue syndrome with an outdated metaphor. While it may be that the illness is not new, correlations with earlier clinical descriptions should not be made merely to reassign a pejorative stigma. This paper continues a tradition of ridiculing chronic fatigue syndrome (2). Considerable progress has been made in understanding many medical conditions previously felt to be of psychosomatic origin. While the etiology of chronic fatigue syndrome may be elusive, it is a syndrome worthy of our research efforts exactly because of its complex nature.

The argument for a medical etiology for chronic fatigue syndrome has been trivialized. No comment is made of the abnormal natural killer cell cytotoxicity (3), immune activation markers (4), and the presence of interferon in CSF (5). An attempt has been made to reduce modern immunologic advances to having "captivated the imagination of both the public and medical professionals." That we do not have full understanding of the role immunology plays in chronic fatigue syndrome should not dismiss its importance. It is not far-fetched to imagine that we are advancing into an era of medical science where symptoms are seen to result from immune system (cytokine) activation rather than the tissue destruction traditionally sought by the pathologist.

It is not the fault of the patient that chronic fatigue syndrome does not fit any conventional disease model. It cannot be seen as an ordinary infectious disease or life-threatening immunodeficiency. But it also cannot be seen as simple depression or a culturally determined illness behavior. The brain is tremendously complex, and modern medicine as a discipline should move beyond the antique dualistic model of "organic" versus "psychologic." The exciting element of science is the possibility to study that which is unknown. The beauty of medicine is to offer compassion without trivializing human suffering with outmoded psychologic constructs. Chronic fatigue syndrome offers us the opportunity to do both.

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DAVID S. BELL, M.D.
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SIR: The recent article on neurasthenia and chronic fatigue syndrome by Drs. Abbey and Garfinkel contains a glaring distortion of the facts. The source of the error is clear from the authors' description of patients with chronic fatigue syndrome as those who are unable to continue full-time work and those who suffer from fatigue, fever, sore throat, muscle aches, headaches, arthralgias without redness or swelling, neuropsychological complaints, and sleep disturbance. In fact, at least 20%-25% of patients with chronic fatigue syndrome are unable to work at all for many years, suffer seizures, and cannot walk normally. In some of these patients the peripheral neuritic pain and myalgia are so severe that suicide may be resorted to. Joint redness and swelling does occur, and patients may become totally economically dependent on their families.

Furthermore, like AIDS, the disease leads to secondary disorders caused by the immune deficiency aspect of the disorder, i.e., thyroiditis, irritable bowel, adrenal deficiency, and, in a number of cases, measurable and observable changes in brain function determined by MRI and PET scan studies of blood flow to the brain (1). Komaroff (2) has studied 350 patients and evaluated 30 epidemic outbreaks. He concluded that the disorder, which may be precipitated by stress or infection, is organic. He discovered that 80% of patients with chronic fatigue syndrome are infected with human herpesvirus type 6 (HHV-6). Hyde (3) has written a scholarly article comparing historically the present epidemic, which the British and Canadians more appropriately label "myalgic myeloencephalitis," to epidemics of poliomyelitis.

From personal observation of 50 cases, it is clear that the discussion by Dr. Abbey and Dr. Garfinkel of chronic fatigue syndrome as a "cultural phenomenon" only addresses the mild form of the disease. In summary, the article is reminiscent of early articles on multiple sclerosis, before it was understood, when it was discussed as an expression of hysteria because it evidenced affective lability and occurred frequently in females.

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SIR: Dr. Abbey and Dr. Garfinkel proposed that chronic fatigue syndrome represents a medical fad and that, like neurasthenia in earlier times, it is the product of an unwitting collusion between physicians and patients.

In contrast to the widespread acceptance the diagnosis of neurasthenia enjoyed, chronic fatigue syndrome has not been a welcome pigeonhole for ambiguous conditions. Derided as the Yuppie flu, it has met with resistance by nonpsychiatric clinicians who tend to invoke psychiatric causes when faced with diagnostic and treatment failures.

There is an urgent issue here that offers a new task for the bioethicist. The assertions of Drs. Abbey and Garfinkel, that "the diagnosis of chronic fatigue syndrome, because of its implied 'organicity,' is attractive to patients and is tenaciously upheld" and, like the neurasthenia it resembles, offers "the only socially legitimate excuse for abandoning the workplace and the pursuit of achievement," risks reinforcing the suspicion of malingering that hangs over chronic fatigue syndrome. Should not Dr. Abbey and Dr. Garfinkel be obliged to comment on their possible reinforcement of this suspicion?

Drs. Abbey and Garfinkel stated, on the basis of data by Kleinman, that "despite pharmacological treatment of the associated psychiatric disorder, neurasthenic symptoms [which they equated with chronic fatigue syndrome] persist." Although this appears strikingly to confirm organicity, the authors concluded that chronic fatigue syndrome is simply "illness behavior" on the ground that, as Kleinman also reported, "only those patients improved who resolved a major family or work problem." (No reason is given not to assume the reverse, that the patient in remission is more capable of resolving family or work problems.)

The finding of Gold et al. (1), cited by Dr. Abbey and Dr. Garfinkel, that there is no difference in HHV-6 antibody titers between chronic fatigue syndrome patients and control subjects, must be compared with the highly significant difference more recently found by Landay et al. (2). Still more recently, Buchwald et al. (3), on the basis of a study of 229 patients, concluded that "the several objective neurologic, immunologic, and virologic findings make a diagnosis of purely psychological illness unlikely," stating further that chronic fatigue syndrome "probably is a heterogeneous illness that can be triggered by multiple different genetic and environmental factors (including stress, toxins, and exogenous infectious agents), all of which can lead to immune dysfunction and the consequent reactivation of latent viruses."

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SIR: In their article on chronic fatigue syndrome Drs. Abbey and Garfinkel argue that the syndromes of neurasthenia and

chronic fatigue share many similarities. They argue critically that both diagnoses reflect the dominant scientific models of the day. Then, using a dominant cultural model—gender—the authors argue that the expanding role of women and conflicts between women's ambition and social possibilities contribute to this diagnosis. They conclude that chronic fatigue syndrome is a culturally sanctioned form of illness behavior and that the majority of these patients suffer from a primary psychiatric disorder.

There are several concerns we have with this article. The authors' conclusions, although reasonable, do not follow from their argument. Although there are similarities between neurasthenia and chronic fatigue syndrome, it does not follow that the two conditions or their fate are the same. Likewise, dominant models, whether they be scientific or cultural, should not be accepted or rejected outright but, rather, need to be carefully evaluated on the basis of available data.

The data that were presented are not convincing. The conclusion that the majority of these patients suffer from a primary psychiatric disorder or depression is controversial. Although Drs. Abbey and Garfinkel cited studies that indicate a high prevalence of psychiatric disorder, especially depression, these studies used instruments—the National Institute of Mental Health Diagnostic Interview Schedule (DIS) and the Structured Clinical Interview for DSM-III-R (SCID)—that were never designed to diagnose psychiatric illness in medically ill patients (1, 2). It remains unresolved whether the so-called vegetative symptoms in these conditions are part of a psychiatric or medical disorder. Likewise, the Hickie study showed that a minority of the patients (45%) had a coexisting major depression and even then it raises the question as to whether this is part of a biological disorder. The role of depression or psychiatric illness is far from clear in these disorders.

The authors too quickly dismiss the biological significance of this syndrome. Many studies report immunological abnormalities in both the humoral and cellular response in chronic fatigue syndrome. The pathophysiology of this syndrome remains unclear. For centuries syphilis was thought to be a psychiatric disorder until *Treponema pallidum* was discovered. Unsuccessful attempts to identify the pathophysiology of an illness does not mean that it is a psychiatric condition, nor can one assume that future research will be unsuccessful.

Our main concern about the article is that the authors appear to eliminate prematurely the biological significance of the syndrome and simultaneously endorse a social and psychological explanation. Our main point is the need for a biopsychosocial approach. This is especially true of chronic fatigue syndrome, which probably consists of a heterogeneous group of illnesses. Progress will be made on the basis of well-designed studies that set out, from an unbiased position, to further clarify and understand the biological, psychological, and social interactions of this complex syndrome.

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SIR: Drs. Abbey and Garfinkel provide an interesting historical review of neurasthenia, but their conclusions about chronic fatigue syndrome seem speculative, demeaning, and inaccurate in the following ways:

1. The authors omitted recent medical research into the etiology of chronic fatigue syndrome. This includes polymer chain reaction techniques that show a possible association between chronic fatigue syndrome and a retrovirus (1) and immune system abnormalities and activation markers (2).

2. The authors failed to examine the research on neuropsychological abnormalities. MRI scans have revealed abnormalities (3), as have single photon emission computed tomography (SPECT) and brain electrical activity mapping scans (4). Reduced ability to acquire new information, as well as drop in IQ, have been seen (unpublished 1989 paper by S. Bastien).

3. The authors concluded that a majority of chronic fatigue syndrome patients will have an identifiable psychiatric disorder. Patients may develop psychiatric difficulties once they acquire chronic fatigue syndrome, but a recent study has shown that the incidence of pre-illness affective or other psychiatric disorders is no greater than in the general population (5).

Our clinical experience suggests that there are substantial differences between chronic fatigue syndrome-related depression and primary major depression. For example, in the former, sleep disorders may involve non-REM sleep rather than the REM disturbance found in major depression (6). The fatigue in chronic fatigue syndrome is accompanied by intense frustration at not functioning well, rather than the apathy and anhedonia experienced by patients with major depressive disorder.

4. The authors imply that chronic fatigue syndrome is both attractive to and has social value for chronic fatigue syndrome patients. This is simply absurd. We have rarely seen secondary gain or social value associated with chronic fatigue syndrome. The price of chronic fatigue syndrome, as with other chronic illnesses, is loss and estrangement from "normal" life. Chronic fatigue syndrome engenders shame, frustration, and stress over not functioning at pre-illness levels.

5. Particularly offensive is the authors' attitude toward women with chronic fatigue syndrome and their conclusion, which is purely speculative and not labeled as such, that chronic fatigue syndrome represents an escape from the stress of balancing work and family obligations. This notion is Victorian. The authors fail to apprise us of how and where they obtained their data on chronic fatigue syndrome, the nature of their study sample, and how they gained their clinical expertise in chronic fatigue syndrome. Finally, how did they conclude that neurasthenia was psychosomatic?

We hope that the authors, in pursuit of their metaphors, will recall Koranyi, who surveyed 4,000 psychiatric patients and found that half had major medical illnesses. One-third of primary care physicians and half of the psychiatrists missed the physical diagnoses.

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SIR: Plaintiffs' attorneys seasoned by clients claiming monies for alleged industrial and similar injuries will spot familiar scenarios among the neurasthenics portrayed by Drs. Abbey and Garfinkel.

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SIR: Drs. Abbey and Garfinkel produced another review linking chronic fatigue syndrome to neurasthenia and proposed that rapid changes in female roles may explain such syndromes. We have demonstrated, however, that any excessive female:male sex ratio is largely an artifact of tertiary referral practice, as the sex ratio in primary care is only 1.3:1 (1). They were dismissive of evidence of immunological dysfunction (2, 3), suggesting that these data simply represent medical fashion. We have demonstrated immunological abnormalities in patients with chronic fatigue syndrome as compared with both normal controls and patients with major depression (2, 4). Further, the demonstration of abnormal cytokine production in patients with chronic fatigue syndrome (5) suggests that an intriguing pathogenesis may underpin "acquired neurasthenia." While no conclusive studies exist, psychiatrists should be more cautious before dismissing such data.

With regard to natural history and treatment outcome, Dr. Abbey and Dr. Garfinkel ignored available studies (1, 6) and relied solely on "clinical experience." Interpretative hypotheses were proposed, despite others' reservations that treatments based on such hypotheses are largely unsubstantiated (7). Pronouncements that improvement depends on resolution of "a major family or work problem" are not consistent with the response of some patients to intravenous immunoglobulin (6).

Although the debate concerning chronic fatigue is one to which psychiatrists should contribute, psychological hypotheses that arbitrarily ignore or discount other models should be avoided. We (8), like others (9), have emphasized the need for collaborative efforts in which immunological, virological, neurohormonal, and psychological hypotheses are evaluated concurrently.

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ANDREW LLOYD
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SIR: Dr. Abbey and Dr. Garfinkel reviewed the similarities between chronic fatigue syndrome and neurasthenia and concluded that, in many cases, chronic fatigue syndrome represents a culturally sanctioned form of illness behavior. Although they acknowledged that a medical basis for chronic fatigue syndrome may be identified in some patients, they argued that the majority of patients suffer from a primary psychiatric disorder, a stress reaction, or a form of illness behavior. They then suggested that this may be due to changes in the role of women and the impact of a materialistic culture.

Although we agree that psychiatrists need to be aware of the possible psychosocial etiology of chronic fatigue, we also feel that it behooves us to be very careful before concluding that a patient's symptoms are largely psychogenic. The psychiatrist must also carefully consider whether the fatigue may be a symptom of an underlying undiagnosed medical illness, such as endocrine disease, HIV infection, Lyme borreliosis, malignancy, mononucleosis, collagen vascular disease, or some other as yet unidentified postinfectious syndrome. Because much in medicine is still unknown, psychiatrists need to maintain an open mind to the multiple determinants of unexplained physical symptoms.

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Dr. Abbey and Dr. Garfinkel Reply

SIR: It is important to address the view that we are "trivializing" or "demeaning" chronic fatigue syndrome by examining the role of culture in the development and popularization of this diagnosis and by comparing it with neurasthenia. In previous work (1) we proposed that chronic fatigue syndrome is a heterogeneous disorder, and we encouraged its study from a variety of perspectives. We advocated the study of both those patients with a primary post-viral syndrome and, what we believe is the larger group, those patients with primary psychopathology or psychophysiological reactions account-

ing for their symptoms. The recognition that many of the patients currently carrying self- or physician diagnoses of chronic fatigue syndrome have underlying psychopathologies is not an invalidation of the existence of the diagnosis in some patients nor is it a trivialization. Rather, it offers the potential of advancing research into the array of disorders that currently fall within the chronic fatigue syndrome rubric. Closer attention to psychiatric and psychosocial factors will allow the detailed study of a more homogenous group of chronic fatigue syndrome patients and is likely to maximize the chance of identifying a pathogenic agent or consistent abnormalities of immune functioning, should they exist, and of correlating these abnormalities with clinically significant variables. The study of those individuals with primary psychopathology will deepen our understanding of the processes of somatization, illness behavior, hypochondriasis, and somatic presentations of the major mental illnesses, all important areas which are costly to society in significant individual and family suffering and use of health care resources.

Dr. Bell's explicit contention and the implicit contentions of Drs. Goodrich and Apfelbaum that conceptualizing chronic fatigue syndrome in some patients as a form of culturally sanctioned illness behavior is consistent with dismissing their suffering reflects a profound lack of understanding of the distress, functional disability, and suffering that are well-documented to be associated with illness behavior (2). Dr. Apfelbaum raises ethical concerns about "the suspicion of malingering which hangs over chronic fatigue syndrome" and asserts that we are encouraging this. While the consideration of malingering or factitious symptom production or reporting may be part of the differential diagnosis for almost any medical condition, we do not believe that a discussion of illness behavior is equivalent to an assertion that patients are malingering. We reject Dr. Bell's assertion that we are "belittling" or "blaming" patients and continuing a "tradition of ridiculing" chronic fatigue syndrome by exploring these themes. His perspective is representative of the larger process of politicization of the diagnosis which only supports research emphasizing the organic aspects of the syndrome (1) and dismisses the important role of psychological factors which are clearly relevant in all medical diseases.

We agree with Dr. Kaplan and colleagues that the role of depression or psychiatric illness is far from well defined, and we have discussed the complex relationship between depression and chronic fatigue syndrome elsewhere (3). This is a subject which is benefiting from improved research methodology, including the use of case definition criteria for chronic fatigue syndrome and an improved understanding of the role of instruments such as the DIS and SCID in the psychiatric assessment of medically ill patients.

We reject Dr. Goodrich's assertion of a "glaring distortion of the facts" and his personal belief in a more severe form of the illness accompanied by seizures and joint redness and swelling, for which there is no scientific support in peer-reviewed publications.

Finally, it has been asserted that we have too quickly dismissed the biological significance of the syndrome. We must emphasize that it was *not* the purpose of the article to critically review the biological research literature. The biology of chronic fatigue syndrome is a complex and problematic area characterized by significant difficulties in research design and methodology which has, to date, produced few studies with solid, replicable findings or findings that correlate with clinical status. The references cited by the correspondents demonstrate many of the problems of research in this area. Due to the limitations of space, we cannot fully critique all of the studies here but will cite a few examples. The finding of Lloyd et al. (Dr. Bell's reference 5) of

elevated interferon-alpha in chronic fatigue syndrome patients is no longer statistically significant when an appropriate Bonferroni correction is made for the multiple comparisons undertaken. The finding did not correlate with duration of symptoms or severity of disability, and in their discussion Lloyd et al. noted that other investigators had either not found this abnormality or demonstrated it in only a small subgroup of chronic fatigue syndrome patients. Klimas et al. (Dr. Bell's reference 3) also noted the variability in findings between investigators. Goldstein's report (Dr. Goodrich's reference 1) and Bastien's report (cited by Ms. Saltzstein and associates) have yet to be described in a peer-reviewed forum. Hyde's study (Dr. Goodrich's reference 3) involved a nonblind assessment of patients, emphasized subtle neurological abnormalities although the patients were not examined by a consultant neurologist, and focused on an epidemic which has unclear relevance for the current sporadic form of the illness. There are no replicated studies that have convincingly demonstrated a viral etiology for the disorder. As with Epstein-Barr virus, it now appears that the primary infection with HHV-6 occurs in most individuals in early life, and the meaning of HHV-6 reactivation in approximately 70% of the subjects of Buchwald et al. (Dr. Apfelbaum's reference 3) is unclear. As they note, it may be an epiphenomenon, secondary to immune dysfunction or have no relation at all to a patient's symptoms. To date, there has been a failure to replicate the retroviral findings. Significant abnormalities of neuropsychological functioning have not been reported in peer-reviewed publications (4). Our own work has documented abnormalities on SPECT scanning in a subgroup of patients with chronic fatigue syndrome but the significance of this finding is unclear (5). Moldovsky's report (Ms. Saltzstein and associates' reference 6) focused on a small number of patients, and studies are currently underway in a number of centers that document a wide range of abnormal sleep findings. No studies in the literature have used adequate psychiatric control groups, which would be an important consideration given the documented abnormalities in immunology, neuroimaging, and neuropsychology that have been found in major depression (3). We are currently pursuing investigations of patients with chronic fatigue syndrome and those with major depression on a variety of immunologic measures in order to help clarify this issue.

Clearly, it is important to study this syndrome further from an integrative biopsychosocial approach using well-designed studies. In this paper, we sought to emphasize the importance of studying social factors in the genesis and shaping of chronic fatigue syndrome.

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Pharmacotherapy of Agitation in Dementia

SIR: We appreciate the carefully designed study by Emil F. Coccaro, M.D., and associates (1) that reported the relative efficacy and side effects of three pharmacotherapies of agitation in dementia. The authors mustered a large sample of well-assessed patients with severe dementia, screened them meaningfully for the independent variable, allowed for dosage adjustment, maintained double-blind conditions, and attended to the validity of the rating process. Their discussion of the background and results anticipated the publication of a scholarly review (2) that provides useful context for such discussion.

Despite the strengths of parallel-group studies in this area, they have major drawbacks in application to individual patients. A physician eager to use these results for a difficult patient would need to know whether his patient belonged to the universe of patients screened and included in this study. If his patient had one of the less common forms of dementia included (for instance, Korsakoff's), he would not know whether the mean outcome data of the whole group had predictive value in his situation. He also would not know from a parallel-group study (as these authors pointed out) whether their finding of "no difference between medications" applied to any individual case.

We recently completed a series of intensive (N-of-1) studies (3) designed to avoid the problems of using extensive study results (paper in preparation). Like Dr. Coccaro and associates, we treated dementia patients with oxazepam and diphenhydramine and used thiothixene instead of haloperidol. We also maintained double-blind conditions and used frequent ratings (shift-by-shift ratings of resistiveness). We crossed over between optimal dosages of each medication often enough to provide several presentations of the most effective.

We found that this strategy was practicable and well accepted in our setting. Of 10 patients admitted, seven remained free of serious medical illness long enough to analyze. One patient was dropped due to improvement during placebo administration. Another did not respond to thiothixene, oxazepam, or diphenhydramine. Of the remaining five, four responded best to thiothixene, 2-4 mg/day, and one responded equally to diphenhydramine, 150 mg/day and thiothixene. None were improved on treatment with oxazepam. Global ratings before and after these trials confirmed that improvement was not achieved by sedation. These findings were transmitted to the clinical team as medication recommendations. Born of long and methodological observation, they survived the inevitable next episodes of resistiveness. In 1- to 2-year follow-up, these medication assignments have, in general, been followed.

Our aggregate results closely mirror those of two reviews of medication trials for agitation in demented patients (4, 5). Antipsychotics have the best, but modest, efficacy, whereas benzodiazepine sedatives have little to offer.

We believe clinical decisions should be guided by the widest experience with similar patients, but behavior disorders in dementia often pose challenges that defeat this guidance. Under such circumstances, an N-of-1 trial may be a reasonable approach. For research use, it may provide (as in this case) treatment evaluation that is economical; for clinical purposes, it may instill confidence that the final treatment is indeed optimal in the long run.

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Dr. Coccaro and Dr. Mohs Reply

SIR: We agree with Dr. Herz and associates that the response of demented patients to various pharmacotherapies for agitation may be highly individual. Given our current state of knowledge, the N-of-1 crossover treatment studies they propose may be the most practical way to identify the best treatment for a single patient. The need for such an approach, however, is a reflection of our poor understanding of "agitated" behavior both biologically and behaviorally. The patients included in our study and in others undoubtedly had a variety of neuropathologic and neurochemical abnormalities. The associated behavioral problems included verbal and physical aggressiveness, pacing, wandering, and anxious and other behaviors. Whether biologic, behavioral, or clinical diagnostic variables could be used to select the most effective agent for a given patient or subgroups of patients remains to be determined. At present we know of no studies demonstrating such treatment specificity. We would like to add that our own study indicates that oxazepam and diphenhydramine are of use for at least some patients.

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ECT and Delirium in Parkinson's Disease

SIR: Jaehoon J. Oh, M.D., and associates (1) described the development of a reversible delirium in seven of 11 patients with Parkinson's disease treated with ECT for "psychiatric illness." In six patients, delirium was so severe that ECT had to be discontinued. They considered the possibility of "a particular vulnerability to the cognitive side effects of ECT" in this patient population. They, however, did not report the medication status of their patients, which may be a factor in their observations.

The response of Parkinson's disease to ECT is reported to be related to an increase in dopamine levels or enhanced dopamine receptor sensitivity (2). Evidence from the animal literature supports this hypothesis (3). Should dopamine transmission, or brain levels of dopamine, become excessive, a delirium or toxic psychosis, such as the one observed with excessive dosages of dopamine agonists, may be precipitated (4). Our preliminary results indicate that coadministration of ECT and antiparkinson agents increases the likelihood of de-

lirium (5). Reducing these agents to one-half their dosage prior to initiating ECT prevented the occurrence of such toxicity without compromising the motoric improvement of Parkinson's disease.

We suggest that standing dosages of dopamine agonists be reduced prior to initiating ECT in order to decrease the incidence of delirium described by Dr. Oh and associates.

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SIR: In a recent communication to the *Journal* (1), we reviewed the evidence for enhanced dopaminergic neurotransmission following a course of ECT (2, and unpublished work of Rudorfer et al.) and wondered whether this could explain the delirium seen in a patient taking dopaminergic medications following completion of ECT. Illustrating our point is the patient series reported recently by Dr. Oh and associates. They described a retrospective analysis of 11 patients with Parkinson's disease who underwent ECT for associated mood disorders. Although most patients benefited from the treatment, they demonstrated an unexpectedly high (64%) incidence of post-ECT delirium, requiring the discontinuation of ECT in six patients.

One explanation for this untoward reaction to convulsive therapy could lie in the concurrent L-dopa-carbidopa combination taken by most of the patients. Enhanced responsivity of dopamine receptors, which has been demonstrated following ECT in parkinsonian as well as depressed patients (2), could excessively potentiate the effects of the dopamine precursor, L-dopa. Moreover, the patients with organic hallucinosis and mania may have had excessive dopaminergic transmission at baseline. While ECT typically exerts an antipsychotic clinical effect, presumably through direct or indirect inhibitory actions on mesolimbic dopamine pathways (our unpublished work), the impact of simultaneous dopaminergic medications is unknown. Also at issue is the question of whether ECT-associated increased permeability of the blood-brain barrier could influence the rate or extent of entry of concurrent medications into the central nervous system.

While Dr. Oh and associates limited their references of ECT use in Parkinson's disease to case reports from the 1970s, the more recent literature includes two highly successful trials of ECT in depressed patients with Parkinson's disease (one reported in the *Journal* [3]), including the only sham-ECT controlled trial (4). While the primary clinical intent was treatment of the mood disturbance, significant concomitant

improvement in the motor signs of Parkinson's disease was also observed (3, 4). Further trials are indicated to define the role of ECT in the treatment of Parkinson's disease (5) with or without associated mental disorders, including the potentially therapeutic or toxic contribution of concurrent medications.

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MATTHEW V. RUDORFER, M.D.
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WILLIAM Z. POTTER, M.D., PH.D.
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SIR: We read with great interest the recent report by Dr. Oh and associates. The authors observed a high incidence of ECT-induced delirium in patients with Parkinson's disease. Consistent with their observations, we recently described the development of an interictal ECT-induced delirium in seven consecutive depressed patients with Parkinson's diseases who received ECT (1). The deliriums were clinically significant, lasting between 7 and 21 days after the ECT was stopped, and were characterized by a substantial lowering of Mini-Mental State Examination scores (mean=11, range=10-23). For the entire group, the number of ECT treatments administered after the onset of the deliriums correlated with the durations of the deliriums ($p=0.03$). There did not appear to be an association between the onset or duration of the delirium and the patient's age, duration of Parkinson's disease, or the daily dosage of L-dopa.

To further examine the incidence of ECT-induced interictal delirium in patients with Parkinson's disease, we recently completed a prospective study that compared the incidence of delirium in 20 depressed patients with a history of a cerebrovascular accident with 20 age-matched depressed Parkinson's patients. The ECT technique has been previously described (1) and was identical for both groups of patients. The diagnosis of ECT-induced delirium was made by a physician on the ECT service on the basis of information obtained from the clinical treatment team and from the serial mental status examinations. The pre-ECT Mini-Mental State scores were similar for both groups (mean=27.2 for patients with cerebrovascular accident versus mean=27.6 for patients with Parkinson's disease).

An interictal ECT-induced delirium occurred in five (25%) of 20 patients with cerebrovascular accident compared with 17 of 20 (85%) patients with Parkinson's disease. A preliminary analysis of the data did not reveal a significant correlation between the time of onset or duration of the deliriums and the patients' sex, daily dosage of L-dopa, or duration of Parkinson's disease. All of the Parkinson's patients received right unilateral electrode placements during ECT. The deliriums all appeared

reversible, but varied in length between 7 days and 3 months after the completion of ECT. Given these findings, it does appear that an ECT-induced delirium occurs more commonly in Parkinson's patients than in patients with cerebrovascular accident (1) or other neurologically healthy, elderly, depressed patients (2, 3).

Since ECT is an effective treatment for both the affective and motor symptoms of Parkinson's disease, further work is needed to identify ways to minimize the encephalopathic side effects of ECT in patients with Parkinson's disease while maintaining the therapeutic advantages of the treatment.

Future studies should examine the potential role that structural brain changes, along with certain clinical and ECT measures, such as electrode placement, ECT medications, frequency of treatment, and the electrical charge, may play in the pathophysiology of ECT-induced delirium (2-4).

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Dr. Oh and Associates Reply

SIR: We were pleased to receive such a robust response to our letter. Drs. Zervas and Fink and Dr. Rudorfer and colleagues raise the question of the possible role of increased L-dopa-generated dopamine activity in the development of delirium in Parkinson patients receiving ECT. In our study, not all patients who experienced post-ECT delirium were taking L-dopa; two of seven patients were not receiving this medication. However, three of the four patients who were free of post-ECT delirium were receiving L-dopa (with carbidopa).

The suggestion that dopamine-active medications be decreased before ECT is appropriate. This has been our standard practice. In fact, our initial approach in treating psychotic Parkinson patients is to decrease anti-Parkinson medications (and other psychoactive drugs) to as low a level as tolerated prior to any other form of treatment.

Dr. Figiel cited two studies consistent with our observations that Parkinson patients experience ECT-induced delirium. In view of the concerns about dopamine-active medications, it is appropriate to point out that the daily dosage of the dopamine agonists administered in those studies tended to be independent of the development of delirium.

ECT-released dopamine should have an extremely short half-life, measured in minutes to hours. Therefore, we question whether ECT-released dopamine could singularly be the cause of delirium persisting for as long as weeks after ECT.

The speculation that an altered blood-brain barrier could be responsible for the delirium is intriguing. Increased passage of L-dopa across this barrier could account for both the delir-

ium and the improvement in Parkinson symptoms. However, one must not lose sight of the fact that carbidopa should also gain access to the central nervous system (CNS) if the blood-brain barrier is damaged. This could offset the effects of increased CNS L-dopa. Carbidopa blocks dopa-decarboxylase, thereby blocking the effects of L-dopa. Normally, it is excluded from the brain by the blood-brain barrier. If there was significant breakdown of the blood-brain barrier, carbidopa passage could lead to marked deterioration of Parkinson control; this was not observed in any of our cases.

Pre-ECT cognitive status may not be a perfect predictor of post-ECT delirium. Prior to ECT, six of our patients underwent formal psychometric testing. Of the three patients with dementia, only two experienced post-ECT delirium. Consequently, other factors such as changes in levels of other neurotransmitters (1), preexisting structural abnormalities (2), and ECT treatment variables may contribute to the development of post-ECT delirium.

Despite the emphasis placed on the delirium that developed in our Parkinson patients, we should not lose sight of the fact that ECT was an effective form of treatment in the majority of our patients. This population of patients presents physicians with difficult treatment dilemmas. We believe that ECT remains an appropriate therapeutic choice in properly selected patients. We concur with Dr. Figiel that further investigations should be directed at the causes of post-ECT delirium to better refine this useful treatment modality.

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A Second Look at the Placebo Response

SIR: In a recent letter, Dr. Frederick J. Lichtigfeld and Dr. Mark A. Gillman proposed that an endogenous opioid system may be involved in the placebo response (1). They cited their work in dealing with alcohol withdrawal states.

In fact, in 1978 Levine and associates (2) suggested the possible role of endogenous endorphin release in mediating placebo response. They studied the effect of naloxone, an opiate antagonist, on dental postoperative pain. Under double-blind, randomized conditions, patients were given either naloxone or placebo several hours after extraction of impacted molars. Patients receiving naloxone reported significantly greater pain than those given placebo. Placebo nonresponders had almost the same postoperative pain levels as those receiving naloxone. In addition, naloxone reduced the prior positive response in patients who had initially responded to placebo. They concluded that endorphin release mediated placebo analgesia in their sample of patients.

Placebo responders are often overlooked in experimental studies. Yet a better understanding of the placebo response would allow for therapy to be more targeted. This would help to avoid the use of unnecessary medication and minimize as-

sociated side effects. The response is complicated and seems to involve a number of biological and psychosocial variables (3, 4). Whether a final common pathway involving the opioid system is found remains to be seen. In addition, the mechanism of the placebo response may vary with the behavior or condition being studied. Perhaps a different set of substances is involved when examining antidepressant response and alcohol withdrawal or pain control. The placebo response deserves more intensive study.

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Dr. Lichtigfeld and Dr. Gillman Reply

SIR: We thank Dr. Lavin for his comments on our letter. Dr. Lavin cites the work of Levine et al., who suggested the role of the endorphins in mediating placebo responses in 1978 (his reference 2). However, these authors only postulated that the endorphins might mediate one aspect of the placebo effect, namely placebo-induced analgesia. We did not claim priority for their suggestion because we were dealing with another condition, namely the placebo response in alcohol withdrawal, in which we postulated the possibility that the endorphin system might also be involved. From our work we then generalized to states of mood, in which we suggested that the endorphins could be involved in placebo responses related to mood disorders generally.

The possibility mentioned by Dr. Lavin, that all placebo responses might be mediated by a final common pathway via the endorphins, may be a premature assumption. Recent work has implicated the serotonergic system in a study comparing vitamin B₆ and placebo in premenstrual tension syndrome in which both agents were equally effective (1). However, the latter work does not exclude the possibility that the endorphin system is also involved in placebo responses to therapy in this condition (1).

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DR. MARK A. GILLMAN
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Sociocultural Perspectives on Substance Abuse Disorders

SIR: I wish to express appreciation and concern regarding the article on substance abuse disorders by the Group for

the Advancement of Psychiatry (GAP) Committee on Alcoholism and Addictions (1).

The article provided an excellent summary of medical perspectives on these disorders yet also seemed distressingly deficient with regard to sociocultural perspectives. Moreover, it seemed embedded in, and thereby perpetuates, the prevailing American ethnocentric, sociopolitical economic ideology that unconsciously dominates so much thinking about and response to addiction. As such it epitomized APA President, Lawrence Hartmann's concern, voiced in a recent *APA Monitor*, that "psychiatry as a model of illness and wellness has shrunk back from biopsychosocial integration toward the narrower, physiologic medical model."

To summarize some relevant issues very briefly, it is increasingly clear that there is wide cross-cultural variation in the acceptability and complications of specific drugs. For example, the introduction of alcohol to tribal peoples has proved widely disastrous, whereas psychedelics used in ritual sacred contexts, such as the Native American Church, apparently lead to little abuse and are regarded as sacramental and therapeutic. Important determinants of a drug's acceptability include not only its morbidity and lethality, but also socioeconomic and political factors such as how long a drug has been available in society, how deeply ingrained its use and sale are in the economy, and whether members of the ruling class are addicted to it. Such factors help answer conundrums such as why we currently spend millions of dollars annually to curtail the use of marijuana, which has an extremely low mortality (zero deaths attributed to marijuana use alone in 1985 is the most recent figure I have seen), yet subsidize growers of tobacco, which causes an extremely high mortality.

The omissions in the article are striking. There was no attention given to nicotine addiction even though it claims over 300,000 lives each year in this country alone. Compare this with the 6,000 deaths per year cited in the article for the total number of deaths (in 1980) from *all* illicit drugs combined and it becomes apparent that something in this article and our collective thinking is tragically amiss.

Social, political, and economic factors also determine which etiological factors are emphasized, e.g., poverty or criminality, and whether resources go predominately toward legal intervention, as they do in the United States, or to the medical and mental health communities for treatment.

It is therefore striking that the article failed to discuss in any depth the relationship of addiction to socioeconomic factors. Yet much drug addiction is clearly a function and symptom of such social ills as poverty, deprivation, and alienation. To fail to address these adequately is to fail the poor.

These omissions bring to light another implicit assumption in the article; namely that psychiatry's proper role is almost exclusively the treatment of individual addicts. Obviously this role is crucial. Yet it may be only by additional preventive intervention in the political and educational domains to ameliorate social, economic, and ideological causes that we can hope to be widely effective in the prevention and treatment of substance abuse disorders.

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Dr. Westermeyer Replies

SIR: Dr. Walsh's comments provide a welcome opportunity for us to elaborate on certain points raised by the paper on substance abuse disorders prepared by the GAP Committee on Alcoholism and Addictions.

Our report was addressed primarily to our colleague-readers in North America, rather than to an international audience. Several of our committee members have had considerable research and consultative experience in Asia, Europe, and Latin America, as well as experience with diverse socioeconomic groups in North America (see works by Blumenthal, Francis, Galanter, Khantzian, Miller, Millman, Nace, Tamerin, Westermeyer). Consequently, we were not unmindful of the sociocultural issues raised by Dr. Walsh, nor are we unconcerned with them. However, we had to select topics that the broad mainstream of our psychiatric colleagues could identify as useful to them in their daily work. There was no effort to cover the entirety of the alcoholism-addictions field in one article.

The issue of tobacco raised by Dr. Walsh is well taken. Certainly, tobacco dependence is a major health threat facing our society. However, its current relevance to many psychiatrists is at issue. *DSM-III-R* criteria for nicotine dependence require advanced pathology along with inability to quit despite medical advice. Nicotine use, abuse, or dependence without a diagnosable condition plus inability to quit after physician recommendation are not diagnosable conditions under *DSM-III-R* criteria. *ICD-9* does not go even as far as *DSM-III-R*. We considered raising these issues regarding nicotine, but a single, focused article was not felt to provide sufficient space to address this important matter in the thorough fashion that it deserves.

We would take issue with Dr. Walsh's innuendo that cannabis abuse and dependence is not a problem in the United States. As clinicians, we regularly see patients whose lives have been adversely affected by cannabis. Clinical surveys over the last two decades have shown that cannabis is second only to alcohol as a substance of abuse in the United States. We would like to see Dr. Walsh's source for the statement "zero deaths attributed to marijuana use alone in 1985." Deaths do occur from suicide, vehicular accidents, other accidents, and homicide in association with cannabis use. Autopsy protocols do not routinely call for cannabis determinations in cases of violent or uncertain death, any more than they require routine nicotine determinations. Were such protocols in place, we might well obtain a clearer picture of cannabis-related problems in the United States. Cannabis-induced fatality in aviation has been documented.

As the newest GAP committee to join that august body, we on the Alcohol Addictions Committee take the charges listed by Dr. Walsh seriously. We do indeed plan to address socioeconomic and sociocultural dimensions of substance-related disorders in our society, including nicotine addiction. By the same token, we believed that in preparing our first report we should begin our quest to influence the minds, hearts, and professional behaviors of our psychiatrist-colleagues by going to those areas of clinical concerns faced daily by them, rather than starting with our concerns, many of which closely match those listed by Dr. Walsh.

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Cocaine Abstinence: "Withdrawal" or Residua of Chronic Intoxication?

SIR: I am pleased to learn that Sally L. Satel, M.D., and colleagues (1) have replicated and expanded our group's find-

ings regarding clinical phenomenology experienced by cocaine addicts during short-term abstinence (2). After reviewing results of both studies, I find that the term "withdrawal" has interfered with our understanding of addiction to stimulants. As noted, our group preferred "short-term abstinence" to "cocaine withdrawal." The issue is conceptual—not just semantic. A traditional sense of "withdrawal" in addicts is probably specific to depressant drugs and is derived from a seminal study by Himmelsbach (3) with opiate addicts and, to a lesser degree, from studies of short-term abstinence syndromes in alcoholics (4). In classic withdrawal, addicts notice *rebound hyperexcitability* (5) during which they experience increased dysphoric psychophysiological phenomena in a matter of hours or days following cessation of a substance. There is a crescendo of distress followed by defervescence of symptoms and signs over days to weeks. In the study of Dr. Satel and colleagues (1) and our study (2), there were linear-like decreases in symptoms over several days with greatest distress noted during use and the immediate postcessation period. In essence, abstinence phenomena reported by our residential subjects were a carryover of *chronic intoxication* effects probably combined with a minimum of conditioned phenomena.

We need to better understand the phenomena of chronic intoxication in addict populations. This would include not only study of neurophysiological effects (i.e., effects of receptor wear and tear as presented by Dr. Satel and colleagues) but also the interplay among adverse medical, legal, social, and occupational consequences and central nervous system changes. In contrast to withdrawal and early abstinence syndromes, periods of chronic intoxication range from months to years. For a frame of reference, one might conceptualize that a course of chronic substance intoxication exists in three phases. The early phase consists of primarily euphoria, few adverse consequences, and establishment of conditioned learning (6). Midphase is the time when there is a decrement in euphoria intensity with continued use of a substance and increased dysphoria secondary to neurophysiological changes and environmental consequences. Late phase consists of minimal euphoria following administration of a substance and growing dysphoria (dopamine depletion?) that becomes intolerable, causing the addict to cease substance use, seek treatment, or accept refuge as a modestly paid residential-research subject. Clinicians are familiar with addicts in the late phase of chronic intoxication who voluntarily seek treatment not because they are in a situational crisis, but because they are "tired."

Hopefully, future research regarding chronic intoxication will help to better understand abstinence phenomena in order to develop interventions more specific to the clinical course of addiction disorders.

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Does Light Therapy Present an Ocular Hazard?

SIR: The literature now reports several promising applications of artificial bright light for treatment of winter depression and various circadian rhythm disturbances. A recent letter (1) reported the case of a patient suffering from premenstrual syndrome who was scheduled for such treatment. Light therapy was withheld, however, because ophthalmological tests revealed retinal pathology.

We would like to reinforce the authors' concern. First, one wants to avoid ascribing preexisting retinal pathology to light treatment. Second, protracted use of artificial bright light might exacerbate certain preexisting retinal lesions. Both practical and theoretical implications have been the focus of a recent detailed review (2). Nevertheless, debate continues among light therapists as to whether patients should routinely be prescreened by an ophthalmologist (3).

There should be no lingering doubt that a basic ocular screening (4) is an essential safety precaution. In routine clinical practice, the patient can complete the eye exam externally and submit the chart. The field still needs to elucidate specific contraindications. There is no long-term experience with light treatment, and all conclusions pointing to innocuousness of the procedure (2) have been based on relatively short-term evaluations.

Is there a relation between bright light exposure and retinal pathology? Long-term light exposure may be a factor contributing to normal retinal aging, age-related degenerative diseases, and certain inflammatory responses (5). Light of even moderate intensity can elicit biochemical cascades that generate potent mediators of degenerative and inflammatory cellular responses (6).

Patients with various retinal diseases and pterygium (which is conjunctival) have inquired whether they are suited for light treatment. The diseases have included background diabetic retinopathy, cystic macular edema, lattice degeneration, early stage hypertensive retinopathy, chorioretinal scars, optic nerve head swelling, and pterygium. Many patients with glaucoma have been routinely excluded. Although there is no evidence that diabetic retinopathy is exacerbated by light, its pathogenesis is still only partially understood. Late stages of retinopathy are among the leading causes of blindness in the Western world, and some of the associated inflammatory-like responses might conceivably increase with light exposure. Cystic macular edema has been noted frequently after exposure to sunlight or artificial light sources (5). It is well-known that pterygia occur more frequently in people exposed to high levels of environmental light. It is unknown whether glaucoma is related to light exposure; light-sensitive neuromodulators or neurohormones (melatonin and dopamine), however, may be involved in regulation of intraocular pressure.

With the spreading application of bright light treatment, the number of such anecdotal reports of ocular pathology is

bound to increase. Similarly, preexisting ocular pathology will be falsely attributed to light treatment. If an ophthalmologist evaluates such patients, supervised use of light therapy becomes possible for many who would otherwise be excluded. Ophthalmological screening—which is quite routine—seems to us mandatory. This should be followed by ophthalmological surveillance of light-treated patients with retinal pathology.

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An Ethnological Approach to Self-Injurious Behavior

SIR: Ronald M. Winchel, M.D., and Michael Stanley, Ph.D. (1), reviewed the data on self-injurious behavior, with regard to its psychodynamic and biological aspects. They found that self-injurious behavior occurs among mentally retarded individuals, psychotic patients, prison populations, and individuals with severe character disorders. The authors state that “self-injurious behavior is a dramatic but poorly understood phenomenon” and “occurs in a variety of clinical settings, and features of the behavior vary among these settings.”

In their review, the authors did not mention cases of self-mutilating behavior that occurred during ancient Mediterranean “rites.” Indeed, in a recent letter (2), we mentioned Sir James Frazer’s work (3), in which the author describes cult worship of the Great Mother Cybele. This cult required its followers to perform ceremonial genital self-mutilation, in recollection of the mythological experience of Attis. Moreover, during this ceremony, the great minister of the cult would cut the skin of his own arms, as a symbolic repetition of his own previous genital mutilation, and sprinkle his blood over the followers in symbolic communion with the Great Mother.

This pattern of religious behavior suggests a similarity with the case reported by Kafka (4), in which the author suggested that the blood may be linked to his patient’s internalized representation of her mother.

In our view, self-injurious behavior may be considered equivalent to genital self-mutilation and should be conceived as an attempt to return to the mother’s womb in the context of a schizophrenic regression (5).

Indeed, studies in cultural anthropology tend to show that

much of man’s behavior and many of his beliefs as to the proper way to satisfy biological needs depend upon the particular sociocultural and religious “milieu” into which he is born (6). Since the combination of social science and psychoanalytic theories has made important contributions to understanding human behavior, we would like to underline the importance of the ethnologic approach to the poorly understood phenomenon of self-injurious behavior.

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Dr. Winchel and Dr. Stanley Reply

SIR: We are grateful to Dr. Novello and Dr. Primavera for raising an interesting aspect of self-mutilation which we chose not to explore in our review, i.e., the role of self-injury in ritual practice. Dr. Novello and Dr. Primavera cite the example of Cybele worship. Multiple examples of ritual self-injury can be found in the cultures of several continents. For readers who are interested in further details regarding the tradition of Cybele and Attis—and for a review of the historical anthropology of self-mutilating behaviors—we recommend Dr. Armando R. Favazza’s excellent book, *Bodies Under Siege* (1).

As Dr. Novello and Dr. Primavera imply, ethnographic variations in psychopathologic behavior should not be overlooked in studies of psychiatric conditions—and too frequently they are. The ethnocentric perspective of many individuals engaged in behavioral research may serve to unintentionally blind us to the variations of behavior that may be found cross-culturally. Awareness of such differences are not only crucial for an empathic understanding of the subjective experience of the patient, but may also serve to highlight certain behavioral features that may merit more detailed attention. Here in the United States, our rich diversity of communities provides us with both the opportunity and responsibility to examine cross-cultural differences.

Despite our agreement with Dr. Novello on this point, in our review we chose not to examine ritual self-injury. In such behavior we considered the locus of motivation to be found, *not* within the individual, but within the group culture. As such, we conclude that despite the topographic similarity of ritual self-injury, it is fundamentally different from the forms of self-injury we did discuss.

Dr. Novello and Dr. Primavera note the similar theme of introjection of the mother found both in the practice of Cybele worship and the speculations of psychodynamic theoreticians regarding the motivation to self-injure. This is an astute ob-

ervation and one that supports the notion that the projective imagery of individuals may be mirrored in the mythic imagery of cultures. But one also wonders, whose imagery is being revealed: that of the patient or that of the psychoanalyst? Despite the heuristic utility of object-relations theory, can its specific symbols—such as merger with the Great Mother—be considered a cult-myth? A deconstructionist examination of object-relations theory may allow us to separate the pure theory from its cultural attributions. As for the ubiquity of Great Mother themes across time and culture—ah, to be Jung again.

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Patients' Appearance and Psychopathology

SIR: The recent letter to the Editor by Justin O. Schechter, M.D. (1), raises several issues which deserve comment. Dr. Schechter suggested that "cosmetic characteristics" such as multiple earlobe piercing or tattoos should not be linked to psychiatric diagnosis. He further described such correlations as "dangerous," a conclusion which seems harsh.

Better observation of patients needs to be encouraged. The initial aspects of the mental status examination involve a general description of the patient (2). This includes details of facial expression, eye contact, personal cleanliness, habits of dress, and motor activity. While this part of the examination is the most straightforward and involves the least interpretation, it seems to be frequently overlooked and inadequately documented. In general, clinicians tend to focus on the more

"positive" or dramatic symptoms of illness such as delusions, hallucinations, or compulsive behaviors. This may lead to the lack of recognition of more subtle pathology such as neuroleptic-induced akathisia or akinesia. It also tends to negate the large influence that appearances play in the rapport of the doctor-patient relationship.

There has been one study of the "tinted-spectacles" sign in which patients who wore sunglasses in the general medical hospital were found to be more likely to display psychopathology (3). Further analysis does suggest that like other signs in psychiatry, the list of possible differential diagnoses is a long one (4). In at least one schizophrenic man, the onset of persistent use of sunglasses was helpful in timing the start of his recent exacerbation. What is important though is that unusual appearances or behaviors be recorded and later questioned taking into account the context in which they appeared.

These observations may not only prove useful in diagnosis, but provide clues to help gauge the progress of treatment. Another patient was noted to no longer cover his ears once his auditory hallucinations had started to subside. While the lack of pathognomonic signs and symptoms is frustrating, better observations will most certainly lead to more definitive treatments.

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Reprints of letters to the Editor are not available.

Annual Index

Following is the comprehensive index for volume 149 of the *Journal*, which covers all material in January 1992 through December 1992. The complete citation for each article in the author index is listed under the name of the first author. Coauthors are listed alphabetically with a cross-reference to the first author; cross-references containing multiple first author names separated by semicolons indicate multiple articles by the coauthor. Book reviews appear in the author index under the name of the reviewer and in the subject index under the heading Books Reviewed; the books reviewed are arranged alphabetically by the surname of the book's first author or editor. In addition to being indexed by author name, letters to the Editor regarding articles published in 1992 are indicated in parentheses after the citations for those articles.

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HALDOL® Decanoate 50 (haloperidol) HALDOL® Decanoate 100 (haloperidol) For IM Injection Only

Brief Summary

The following is a brief summary only. Before prescribing, see complete prescribing information in HALDOL and HALDOL Decanoate product labeling.

CONTRAINDICATIONS: Since the pharmacologic and clinical actions of HALDOL Decanoate 50 and HALDOL Decanoate 100 are attributed to HALDOL haloperidol as the active medication, CONTRAINDICATIONS, WARNINGS, and additional information are those of HALDOL, modified to reflect the prolonged action. HALDOL is contraindicated in severe toxic central nervous system depression or comatose states from any cause and in individuals who are hypersensitive to this drug or have Parkinson's disease.

WARNINGS: Tardive Dyskinesia: Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown. Both the risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown. Given these considerations, antipsychotic drugs should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment should generally be reserved for patients who suffer from a chronic illness that 1) is known to respond to antipsychotic drugs, and 2) for whom alternative, equally effective, but potentially less harmful treatments are not available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically. If signs and symptoms of tardive dyskinesia appear in a patient on antipsychotics, drug discontinuation should be considered. However, some patients may require treatment despite the presence of the syndrome. (For further information about the description of tardive dyskinesia and its clinical detection, please refer to ADVERSE REACTIONS.)

Neuroleptic Malignant Syndrome (NMS): A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status (including catatonic signs) and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmias). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis) and acute renal failure. The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary central nervous system (CNS) pathology. The management of NMS should include 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; 2) intensive symptomatic treatment and medical monitoring; and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS. If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported. Hyperpyrexia and heat stroke, not associated with the above symptom complex, have also been reported with HALDOL.

Usage in Pregnancy: (see PRECAUTIONS - Usage in Pregnancy)

Combined Use With Lithium: (see PRECAUTIONS-Drug Interactions)

General: Bronchopneumonia, sometimes fatal, has followed use of antipsychotic drugs, including haloperidol. Prompt remedial therapy should be instituted if dehydration, hemoconcentration or reduced pulmonary ventilation occur, especially in the elderly. Decreased serum cholesterol and/or cutaneous and ocular changes have been reported with chemically-related drugs, although not with haloperidol. See PRECAUTIONS - Information for Patients for information on mental and/or physical abilities and on concomitant use with other substances.

PRECAUTIONS: Administer cautiously to patients: (1) with severe cardiovascular disorders, due to the possibility of transient hypotension and/or precipitation of anginal pain (if a vasopressor is required, epinephrine should not be used since HALDOL may block its vasopressor activity and paradoxical further lowering of blood pressure may occur; metaraminol, phenylephrine or norepinephrine should be used); (2) receiving anticonvulsant medications, with a history of seizures, or with EEG abnormalities, because HALDOL may lower the convulsive threshold. If indicated, adequate anticonvulsant therapy should be concomitantly maintained; (3) with known allergies or a history of allergic reactions to drugs; (4) receiving anticoagulants, since an isolated instance of interference occurred with the effects of one anticoagulant (phenindione). Concomitant antiparkinson medication, if required, may have to be continued after HALDOL is discontinued because of different excretion rates; if both are discontinued simultaneously, extrapyramidal symptoms may occur. Intraocular pressure may increase when anticholinergic drugs, including antiparkinson drugs, are administered concomitantly with HALDOL. When HALDOL is used for mania in bipolar disorders, there may be a rapid mood swing to depression. Severe neurotoxicity may occur in patients with thyrotoxicosis receiving antipsychotic medication, including HALDOL.

The 1, 5, 10 mg HALDOL tablets contain FD&C Yellow No. 5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible individuals, especially in those who have aspirin hypersensitivity.

Information for Patients: Mental and/or physical abilities required for hazardous tasks or driving may be impaired. Alcohol should be avoided due to possible additive effects and hypotension.

Drug Interactions: Patients receiving lithium plus haloperidol should be monitored closely for early evidence of neurological toxicity and treatment discontinued promptly if such signs appear. As with other antipsychotic agents, it should be noted that HALDOL may be capable of potentiating CNS depressants such as anesthetics, opiates, and alcohol.

Carcinogenesis, Mutagenesis and Impairment of Fertility: No mutagenic potential of haloperidol was found in the Ames Salmonella microsome activation assay. Negative or inconsistent positive findings have been obtained in *in vitro* and *in vivo* studies of effects of haloperidol on chromosome structure and number. The available cytogenetic evidence is considered too inconsistent to be conclusive at this time. Carcinogenicity studies using oral haloperidol were conducted in Wistar rats (dosed at up to 5 mg/kg daily for 24 months) and in Albino Swiss mice (dosed at up to 5 mg/kg daily

for 18 months). In the rat study survival was less than optimal in all dose groups, reducing the number of rats at risk for developing tumors. However, although a relatively greater number of rats survived to the end of the study in high dose male and female groups, these animals did not have a greater incidence of tumors than control animals. Therefore, although not optimal, this study does suggest the absence of a haloperidol related increase in the incidence of neoplasia in rats at doses up to 20 times the usual daily human dose for chronic or resistant patients. In female mice at 5 and 20 times the highest initial daily dose for chronic or resistant patients, there was a statistically significant increase in mammary gland neoplasia and total tumor incidence; at 20 times the same daily dose there was a statistically significant increase in pituitary gland neoplasia. In male mice, no statistically significant differences in incidences of total tumors or specific tumor types were noted. Antipsychotic drugs elevate prolactin levels; the elevation persists during chronic administration. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin dependent *in vitro*, a factor of potential importance if the prescription of these drugs is contemplated in a patient with a previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomastia, and impotence have been reported, the clinical significance of elevated serum prolactin levels is unknown for most patients. An increase in mammary neoplasms has been found in rodents after chronic administration of antipsychotic drugs. Neither clinical studies nor epidemiologic studies conducted to date, however, have shown an association between chronic administration of these drugs and mammary tumorigenesis; the available evidence is considered too limited to be conclusive at this time.

Usage in Pregnancy: Pregnancy Category C. Safe use in pregnancy or in women likely to become pregnant has not been established; use only if benefit clearly justifies potential hazards to the fetus.

Nursing Mothers: Infants should not be nursed during drug treatment.

Pediatric Use: Controlled trials to establish the safety and effectiveness of intramuscular administration in children have not been conducted.

ADVERSE REACTIONS: Adverse reactions following the administration of HALDOL Decanoate 50 or HALDOL Decanoate 100 are those of HALDOL haloperidol. Since vast experience has accumulated with HALDOL, the adverse reactions are reported for that compound as well as for haloperidol decanoate. As with all injectable medications, local tissue reactions have been reported with haloperidol decanoate.

CNS Effects: Extrapyramidal Symptoms (EPS) — EPS during the administration of HALDOL (haloperidol) have been reported frequently, often during the first few days of treatment. EPS can be categorized generally as Parkinson-like symptoms, akathisia, or dystonia (including opisthotonos and oculogyric crisis). While all can occur at relatively low doses, they occur more frequently and with greater severity at higher doses. The symptoms may be controlled with dose reductions or administration of antiparkinson drugs such as benztropine mesylate USP or trihexyphenidyl hydrochloride USP. It should be noted that persistent EPS have been reported; the drug may have to be discontinued in such cases. **Withdrawal Emergent Neurological Signs** — Abrupt discontinuation of short-term antipsychotic therapy is generally uneventful. However, some patients on maintenance treatment experience transient dyskinetic signs after abrupt withdrawal. In certain cases these are indistinguishable from "Tardive Dyskinesia" except for duration. It is unknown whether gradual withdrawal will reduce the occurrence of these signs, but until further evidence is available HALDOL should be gradually withdrawn. **Tardive Dyskinesia** — As with all antipsychotic agents HALDOL has been associated with persistent dyskinesias. Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements, may appear in some patients on long-term therapy or may occur after drug therapy has been discontinued. The risk appears to be greater in elderly patients on high-dose therapy, especially females. The symptoms are persistent and in some patients appear irreversible. The syndrome is characterized by rhythmic involuntary movements of tongue, face, mouth or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes these may be accompanied by involuntary movements of extremities and the trunk. There is no known effective treatment for tardive dyskinesia; antiparkinson agents usually do not alleviate the symptoms of this syndrome. It is suggested that all antipsychotic agents be discontinued if these symptoms appear. Should it be necessary to reinstitute treatment, or increase the dosage of the agent, or switch to a different antipsychotic agent, this syndrome may be masked. It has been reported that fine vermicular movement of the tongue may be an early sign of tardive dyskinesia and if the medication is stopped at that time the full syndrome may not develop. **Tardive Dystonia** — Tardive dystonia, not associated with the above syndrome, has also been reported. Tardive dystonia is characterized by delayed onset of choreic or dystonic movements, is often persistent, and has the potential of becoming irreversible. **Other CNS Effects** — Insomnia, restlessness, anxiety, euphoria, agitation, drowsiness, depression, lethargy, headache, confusion, vertigo, grand mal seizures, and exacerbation of psychotic symptoms including hallucinations, and catatonic-like behavioral states which may be responsive to drug withdrawal and/or treatment with anticholinergic drugs.

Body as a Whole: Neuroleptic malignant syndrome (NMS), hyperpyrexia and heat stroke have been reported with HALDOL. (See WARNINGS for further information concerning NMS.)

Cardiovascular Effects: Tachycardia, hypotension, hypertension and ECG changes, including prolongation of the Q-T interval and ECG pattern changes compatible with the polymorphous configuration of torsades de pointes.

Hematologic Effects: Reports of mild, usually transient leukopenia and leukocytosis, minimal decreases in red blood cell counts, anemia, or a tendency toward lymphomonocytosis; agranulocytosis rarely reported and only in association with other medication.

Liver Effects: Impaired liver function and/or jaundice.

Dermatologic Reactions: Maculopapular and acneiform reactions, isolated cases of photosensitivity, loss of hair.

Endocrine Disorders: Lactation, breast engorgement, mastalgia, menstrual irregularities, gynecomastia, impotence, increased libido, hyperglycemia, hypoglycemia and hyponatremia.

Gastrointestinal Effects: Anorexia, constipation, diarrhea, hyper-salivation, dyspepsia, nausea and vomiting.

Autonomic Reactions: Dry mouth, blurred vision, urinary retention, diaphoresis, and priapism.

Respiratory Effects: Laryngospasm, bronchospasm and increased depth of respiration.

Special Senses: Cataracts, retinopathy and visual disturbances.

Other: Cases of sudden and unexpected death have been reported in association with the administration of HALDOL. The nature of the evidence makes it impossible to determine definitively what role, if any, HALDOL played in the outcome of the reported cases. The possibility that HALDOL caused death cannot, of course, be excluded, but it is to be kept in mind that sudden and unexpected death may occur in psychotic patients when they go untreated or when they are treated with other antipsychotic drugs.

Postmarketing Events: Hyperammonemia has been reported in a 5½ year old child with citrullinemia, an inherited disorder of ammonia excretion, following treatment with HALDOL.

IMPORTANT: Full directions for use should be read before HALDOL or HALDOL Decanoate products are administered or prescribed.

For Information on symptoms and treatment of overdose, see full prescribing information.

The short-acting HALDOL injectable form is intended only for acutely agitated psychotic patients with moderately severe to very severe symptoms.

12/30/91

Reference:

1. Youssef HA. A five-year follow-up study of chronic schizophrenics and other psychotics treated in the community: depot haloperidol decanoate versus other neuroleptics. *Adv Ther.* 1989;6(4):186-195.

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During dose adjustment or episodes of exacerbation of psychotic symptoms, therapy with HALDOL Decanoate 100 or HALDOL Decanoate 50 can be supplemented with short-acting forms of HALDOL[®] (haloperidol). The side effects of the decanoate products are those of HALDOL. The prolonged action of HALDOL Decanoate 100 and HALDOL Decanoate 50 should be considered in the management of side effects.

Please see brief summary of Prescribing Information on adjacent page.